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ORGANIC CHEMISTRY

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FOR

STUDENTS OF MEDICINE

BY

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PREFACE

THE time allotted in an ordinary medical curriculum in this country to the study of Chemistry may not exceed six months. It is plain that in this brief period the student can gain little acquaintance with the subject, and yet when he passes on to the study of Physiology, of Pharmacology, and of Pathology, he is expected to possess a knowledge not only of the simple principles of Chemistry, but a detailed knowledge of numerous substances and processes, many of them very complex in character.

It seems to me that the only way to meet the difficulty here indicated, in default of an extended scientific curriculum, is to select the chemical substances considered in the course, not so much for their importance in systematic or synthetic chemistry, as for their medical interest. Only thus can time be obtained for the study of what will be of some utility to the student of medicine in the later portions of his professional education.

I am convinced by experience that this plan need not involve any diminution in the appreciation of scientific method by the student, while it greatly increases his interest in the subject.

It is my intention to write a complete text-book of Chemistry from this point of view, but meanwhile I make a beginning with the present volume on Organic Chemistry, as the necessity seems here to be greatest. A feature, which I venture to think simplifies the presentation of an admittedly

difficult subject, is the postponement of the consideration of nitrogenous compounds to the last third of the book.

Some may think that I have gone too far by the introduction of sections on complex compounds such as the Proteins, Glucosides, Alkaloids, and Dyes, and that it is impossible for the student to acquire any adequate knowledge of these groups of substances in a first course of Chemistry. Even if this be so, the student should be made to realise that he has not done with Chemistry when he has passed his First Professional Examination. His text-book should not then be discarded, but made use of in his later studies, into which complex problems of Organic Chemistry constantly enter.

EDINBURGH, *August* 1913.

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ORGANIC CHEMISTRY

INTRODUCTORY.

THE term organic chemistry was first employed in opposition or in contradistinction to the term mineral chemistry. Whilst the earlier chemists succeeded in reproducing many mineral substances, they were unsuccessful by laboratory operations in forming the compounds, often very complex, which appeared as constituents of living organisms, whether plants or animals. It was therefore thought that there was some essential difference between these latter, the so-called organic compounds, and the former, the mineral or inorganic compounds. The distinction was broken down once for all by Wöhler in 1828, who succeeded in producing from inorganic material the compound urea, a characteristic product of the animal organism. Since his time many other organic compounds have been synthetised, but we still retain the classification of compounds into organic and inorganic as convenient for educational and descriptive purposes. The terms, however, have lost their original significance, and by organic chemistry we practically mean the chemistry of the carbon compounds. Certain simple compounds, such as the oxides of carbon and the carbonates, are conventionally regarded as "inorganic," and are described in text-books of inorganic chemistry: all other carbon compounds, whether related to living organisms or not, are treated under the heading of organic chemistry.

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PURIFICATION OF ORGANIC SUBSTANCES.

Crystallisation.

When the organic substance to be purified is a crystalline solid it is generally purified by recrystallisation. In the case of inorganic substances water is almost the only solvent used; but organic substances are frequently insoluble in water, so that with them other solvents must be employed. The chief of these are alcohol, ether, benzene, and petroleum ether (p. 104). All of these solvents have boiling-points lower than that of water, so that any solvent which the crystals may retain after separation may easily be removed as vapour. For purposes of purification the selection of solvents may be of considerable importance, for the substance, although soluble in many solvents, may crystallise much more readily from one than from the others.

When the substance, as often happens, is contaminated with tarry material, its solution may be shaken or boiled with purified animal charcoal, which removes the colouring matter from the solution and permits the formation of clean crystals on evaporation or cooling.

Purity of a crystalline organic substance is generally tested by the constancy of its melting-point (p. 8). If the substance melts sharply at a definite temperature and this melting-point does not change after the substance has again been crystallised, the material is generally regarded as pure.

Fractional Distillation.

When the substance is an organic liquid which boils without decomposition, it is often purified by distillation. On a laboratory scale the distillation is generally carried out in the apparatus shown in Fig. 1. The substance to be distilled is contained in the distilling flask F, through the neck

of which a thermometer is introduced. The bulb reaches slightly below the side-tube, through which the vapours of the boiling liquid pass into the condenser C, the condensed liquid dropping into the receiver R. For high-boiling liquids the condenser need only be cooled by exposure to air, but for low-boiling liquids a water-cooled condenser, as represented in the figure, is necessary. In such a condenser a stream of cold water enters through the lower side-tube and escapes through the upper side-tube. The form of condenser here shown is generally known as a Liebig's condenser.

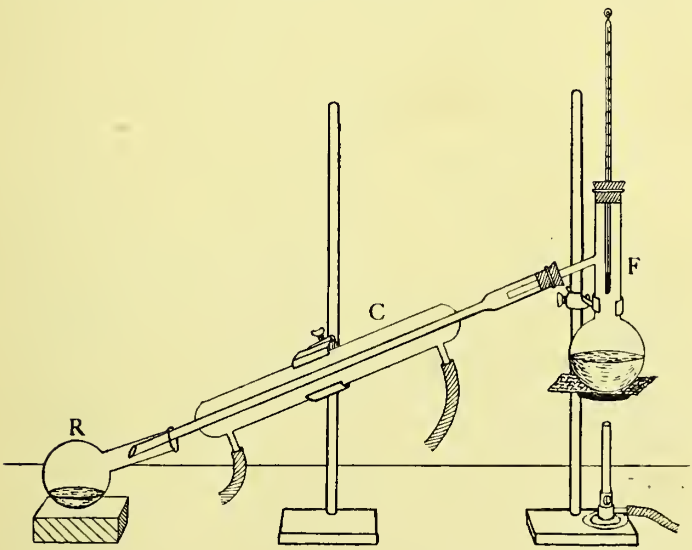


FIG. 1.

If the liquid is pure, it boils over completely at a constant temperature, which is the boiling-point of the pure liquid. If, on the other hand, the liquid is impure, the boiling-point constantly rises, the more volatile impurities, if any are present, coming off at a lower temperature. When these are substantially removed, the boiling-point has risen approximately to that of the pure liquid, which then boils over; and should any less volatile impurities be present, these come over at a higher temperature still. The receiver is changed for the reception of each fraction.

Of course, the separation effected in this way is not sharp,

the rise in boiling-points as registered on the thermometer being more or less gradual, and it may be necessary to collect the distillate in many more fractions than the three indicated above. If the fractional distillation is to be really effective some sort of **still-head** is almost essential. One kind of still-head is shown in Fig. 2. The object of this or similar still-heads is to have a considerable amount of condensation taking place before the vapour ultimately escapes to the condenser. The lower portion of the still-head is fitted through the cork of the distilling flask, and the thermometer is now introduced into the top of the still-head, the bulb as before reaching slightly below the side-tube, which is connected with the condenser. In each pear-shaped bulb of the still-head a certain amount of condensation takes place by air-cooling. In the lowest bulb the least volatile material of the vapour condenses, and the uncondensed portion which passes into the second is on the whole more volatile than the vapour which passes from the original liquid into the flask. In the second bulb, again, there is further condensation of less volatile material, and the vapour which enters the third bulb is more volatile still. By the time the vapour has reached the thermometer it has been deprived by condensation of a large proportion of the less volatile material which the original vapour contained, and which has dropped back through the bulbs and tubes of the still-head to the flask. By the use of such a still-head, then, the separation of the more and less volatile constituents of a mixture is more sharply effected. The receiver at the end of the condenser is changed from time to time, as a knowledge of the boiling-point of the substance and the experience of the operator may dictate. Each fraction collected in this way may be subjected to refractionation and consequent further purification. A constant boiling-point, like a constant melting-point, is taken as a criterion of purity. Since the boiling-point varies somewhat with the atmospheric pressure, this must be taken account of in accurate work.

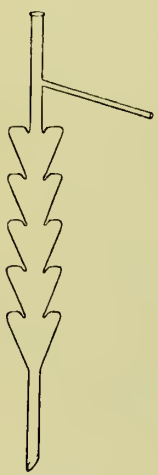


FIG. 2.

Vacuum Distillation.—Since most organic substances are at least partially decomposed by prolonged heating in the neighbourhood of 300°, and many undergo decomposition at temperatures even lower than this, it is often necessary to carry out the process of distillation at a lower temperature than the boiling-point of the liquid under ordinary atmospheric pressure. Since the vapour pressure of all liquids diminishes with fall of temperature, it is possible by suitably lowering the pressure on the liquid to lower the boiling-point by 100° or more under conditions that can be easily attained in practice. Thus glycerine, especially when impure, tends to decompose at its boiling-point, which is 290° at 760 mm. In order, therefore,

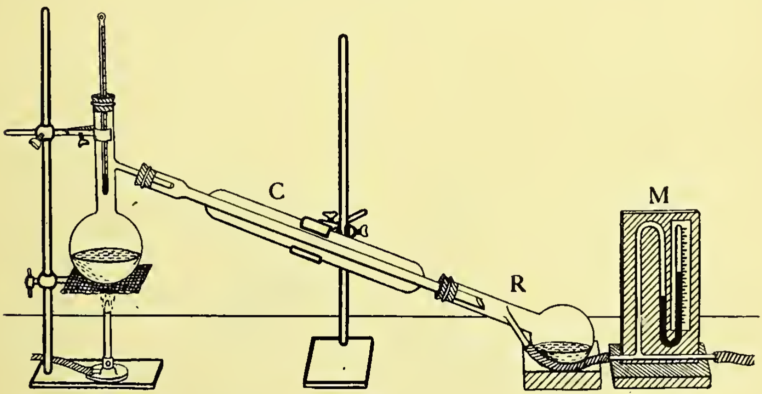


FIG. 3.

to distil glycerine without decomposing it, the operation is carried out in a partial vacuum, the actual boiling-point depending upon the pressure in the distilling apparatus. At 50 mm. pressure glycerine boils at 210°, at 12 mm. pressure it boils at 175°. At these temperatures there is no decomposition, so that the glycerine can then be freely distilled. The latter pressure of 12 mm. can easily be attained in the laboratory by the use of an ordinary suction-pump attached to the water supply.

A form of apparatus for distillation under diminished pressure commonly employed in the laboratory is represented in Fig. 3. The apparatus is set up just as for an ordinary distillation, but the receiver R is fitted tightly to the condenser

C, and is further connected through a side-tube and the manometer M to the pump which exhausts the apparatus. The pressure under which the distillation takes place is registered by the manometer, and is observed at the same time as the boiling-point.

Distillation with Steam.—In the case of liquids which are insoluble in water or nearly so, the process of steam distillation is often adopted. In this process a current of steam is blown through the liquid, and carries over with it as vapour a portion of the substance to be distilled. This vapour is condensed along with the steam, and as the substance is supposed to be nearly insoluble in water, it may be easily separated from the water along with which it condenses. Fig. 4 shows

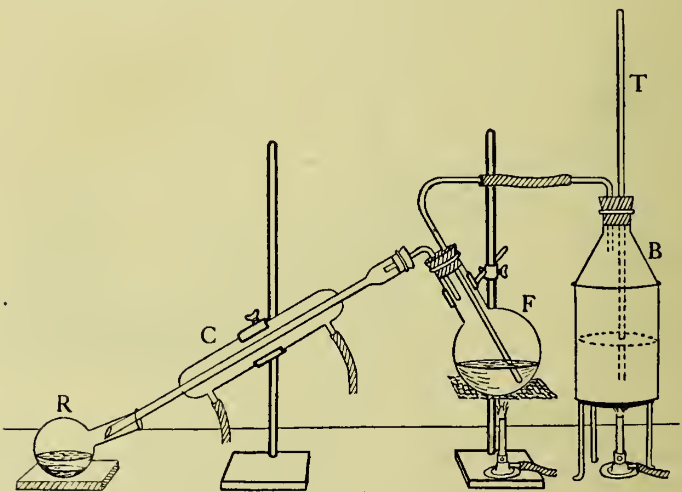


FIG. 4.

an apparatus employed for the purpose in the laboratory. A boiling-can, B, provided with an open safety-tube, T, is used to generate the steam. The steam bubbles through the liquid to be distilled, which is contained in the flask F, and carries along with it some of the vapour of the liquid which condenses along with the steam in the condenser C, and collects as a separate layer or as solid in the receiver R.

This process is practically one of distillation at constant temperature, the temperature in the flask remaining in the

neighbourhood of the boiling-point of water, namely 100°. The operation can usually be carried out successfully if the boiling-point of the liquid to be distilled is under 200°. If it is much above that value its vapour pressure at 100° is so small (that is, so little comes over with the steam as vapour) that the method is not then generally adopted.

DETERMINATION OF MELTING- AND BOILING-POINTS.

Melting-point.—The melting-point of a crystalline organic substance may be conveniently determined by means of the apparatus shown in Fig. 5. The substance is filled into a thin-walled capillary, C, which is attached, usually by means of a rubber band, to the stem of the thermometer T. The capillary is so placed that the substance is on the same level as the bulb of the thermometer. The thermometer and capillary are then made to dip under the surface of a suitable liquid contained in the bulb-tube B. This tube is not tightly closed by the cork, which either fits loosely or is provided with a slit to allow communication with the air. The liquid in B is heated slowly by means of a small flame placed beneath it, and the substance contained in the capillary is kept under constant observation. When the melting-point of the substance is reached, the solid is seen to run together and a clear liquid takes its place. If the substance is pure, the melting-point is quite sharp; if it is impure, incipient fusion takes place at a temperature which may be several degrees lower than that at which the fusion is complete.

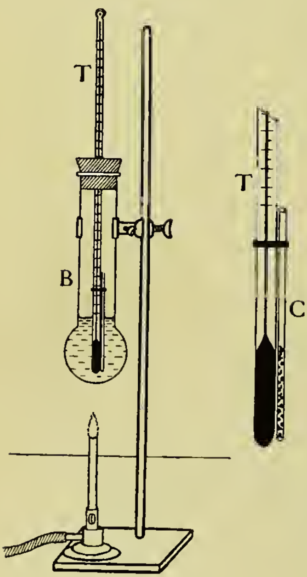


FIG. 5.

The liquid generally used in B is concentrated sulphuric acid, which may be employed up to a temperature of nearly 300°, especially if some potassium sulphate has previously been dissolved in it.

Boiling-point.—The boiling-point is usually determined by means of the apparatus already shown under the heading of fractional distillation. The still-head is not in general necessary for this purpose, and the boiling should be conducted at such a rate that the liquid drops only slowly from the condenser. If the barometric pressure is widely different from the average value of 760 mm., the height of the barometer should be noted and given along with the boiling-point registered by the thermometer. In the case of boiling-point measured under reduced pressure, the apparatus for determining which is represented in Fig. 3, the reading of the manometer must always be given as well as the boiling-point.

If only a small quantity of liquid is available, its boiling-point may be determined by a method analogous to that used for the determination of the melting-point. The apparatus for the purpose is shown in Fig. 6. Attached to the thermometer T by means of thread or asbestos cord is a small bulb of the shape shown in the figure at B, in which the liquid is contained. The external liquid in the beaker is slowly heated, with constant stirring if necessary. As the air in the bulb B expands by the rise of temperature, a succession of small bubbles appears at the open end of the capillary of the bulb. These bubbles succeed each other, however, only slowly. When, on the other hand, the boiling-point of the liquid in the bulb is reached, vapour is produced freely, and a rapid succession of bubbles is observed. The thermometer is then read, and the flame removed. The rapid bubbling continues until the temperature has dropped below the boiling-point, when it ceases, and the thermometer is again read. If the heating and

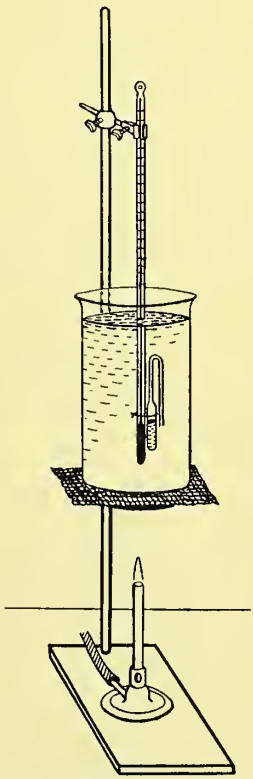


Fig. 6.

cooling have been conducted slowly, the boiling-point may be taken as midway between the two temperatures.

The bulb B is filled by warming it in a Bunsen flame, whilst the open end of the capillary dips under the surface of the liquid to be tested. As the bulb cools the air within it contracts, and liquid flows up the capillary into the bulb. This operation may be repeated if necessary until the bulb is filled to the extent shown in the figure.

ULTIMATE ORGANIC ANALYSIS.

For the purposes of research in organic chemistry, and also for the investigation of the energy requirements of the organism (calorific value of foods, etc.), it is frequently necessary to determine the percentage of the elements composing organic compounds. The chief elements to be considered are carbon, hydrogen, nitrogen, and oxygen. The amount of oxygen is invariably estimated by difference, the amounts of the other elements are determined directly.

Estimation of Carbon and Hydrogen.

For the estimation of carbon and hydrogen the method of combustion is universally employed. A weighed quantity of

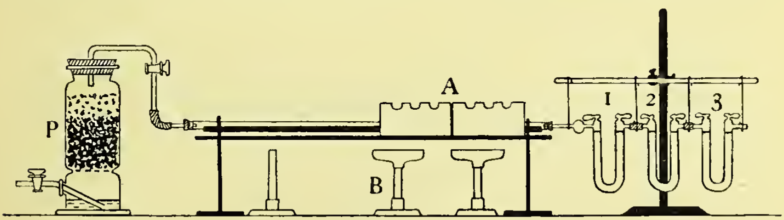


FIG. 7.

the substance to be analysed is burned in excess of air or oxygen. Carbon is thereby converted into carbon dioxide, which is absorbed by potash solution or soda-lime; hydrogen is converted into water, which is absorbed by anhydrous calcium chloride, or pumice-stone soaked in concentrated sulphuric acid. The increase in weight of the tubes containing these absorbents is due to the carbon dioxide and water respectively.

The apparatus employed is sketched above in Fig. 7.

A hard-glass or quartz combustion tube, about 60 cm. long and 1 cm. in diameter, is charged with a column of copper oxide (usually prepared by oxidising copper wire). The

entrance to the tube is connected with a supply of air or oxygen, which is purified by bubbling it first through concentrated sulphuric acid contained in the lower compartment of the purifying tower P, and then through a long column of soda-lime, and a shorter column of calcium chloride in the upper compartment. The air or oxygen is thus freed from moisture and carbon dioxide, and can be used for the combustion. The exit of the tube is connected with U-tubes containing the absorbents. Tube 1 contains calcium chloride to absorb moisture; tubes 2 and 3 contain soda-lime, a little calcium chloride being placed over the soda-lime in the exit limb of each tube to prevent escape of moisture, which might be formed by the action of carbon dioxide on the soda-lime. These tubes are weighed separately before the combustion, and again when the combustion is finished. The increase in weight of tube 1 is due to water, and $\frac{1}{9}$ of this increase in weight, *i.e.* the ratio of H_2 to H_2O, represents the weight of hydrogen in the substance taken. The joint increase in weight of the tubes 2 and 3 is due to carbon dioxide, $\frac{3}{11}$ of which increase, *i.e.* the ratio of C to CO_2, represents the weight of carbon in the substance taken.

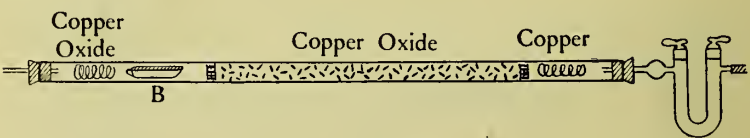


FIG. 8.

The combustion tube is heated in the iron gutter of the combustion furnace by means of Bunsen burners, B, furnished with tops for spreading the flame into a thin sheet, or into a number of small jets arranged longitudinally under the gutter. To conserve the heat, fireclay tiles, or pieces of angle-iron, lined with asbestos and provided with holes in the angle to allow the escape of the gases from the burners, are placed over part or all of the tube, as at A.

The arrangement in the interior of the combustion tube is shown in Fig. 8. The substance to be analysed is either mixed with fine copper oxide, or placed in a porcelain or platinum boat at B. A roll of oxidised copper wire gauze is placed at the entrance of the tube, and in the case of substances containing

nitrogen, a roll of unoxidised copper gauze at the exit. The object of the last is to reduce any oxides of nitrogen which might be formed to nitrogen itself, which is unaffected by the absorbents used to collect the water and carbon dioxide. The column of copper oxide is heated to dull redness in a slow current of air or oxygen, and heat is gradually applied to the substance in the boat, which volatilises and is oxidised either directly by oxygen or by the hot copper oxide over which the vapour passes. Any charred residue in the boat gradually burns away in the current of oxygen.

Estimation of Nitrogen.

For the purposes of organic chemistry, nitrogen is chiefly estimated by means of Dumas's method, which consists in heating a weighed quantity of the substance with copper oxide in a current of carbon dioxide, the apparatus used being a combustion tube and furnace like those employed in the estimation of carbon and hydrogen. The nitrogen of the organic substance comes off as such, and is swept out by the current of carbon dioxide into a measuring tube containing a concentrated solution of potassium hydroxide. The carbon dioxide is absorbed by this solution, leaving the nitrogen, the volume of which may then be measured.

For the purposes of physiological chemistry, however, the method of nitrogen estimation almost invariably employed is that of Kjeldahl. Kjeldahl's method is less accurate than the other in some particular cases, but it is simpler in execution and requires less attention. It is based on the principle that most nitrogenous organic substances when heated with concentrated sulphuric acid have their nitrogen completely converted into ammonium sulphate. The ammonium sulphate may then be distilled with a solution of caustic alkali in excess, when ammonia passes over along with the steam and is absorbed in a known volume of standard acid solution. The quantity of acid neutralised by the ammonia can then be determined by titration of the excess of acid with standard alkali.

The apparatus employed in Kjeldahl's method is shown in the accompanying figures. Fig. 9 represents a hard-glass flask in which a weighed quantity of the nitrogenous substance is heated with a large excess of concentrated sulphuric acid. The

sulphuric acid is boiled in the flask, the mouth of which is closed by a loosely fitting glass bulb to prevent undue escape of vapours, which mostly condense in the neck and run back into the flask. As the action of the sulphuric acid is somewhat slow, means are usually taken to accelerate it. One of these is to add potassium sulphate to the sulphuric acid. This reacts with the acid to form potassium hydrogen sulphate, which, dissolved in the excess of sulphuric acid, greatly raises the boiling-point, so that the reaction takes place at a higher temperature, and is in consequence more rapid. Another device

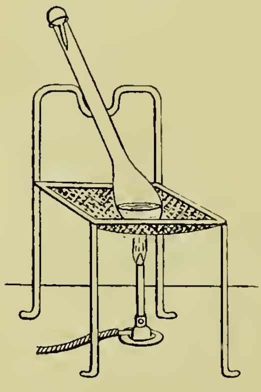


FIG. 9.

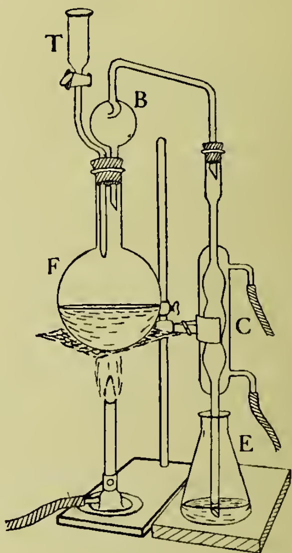


FIG. 10.

to hasten the action is the employment of a catalyst, the substances which are commonly used being copper sulphate or mercuric sulphate. The latter is produced by adding a small globule of mercury to the sulphuric acid.

The organic substance is charred by the hot sulphuric acid, but after a time the solution loses colour, and becomes finally of a pale straw colour or quite colourless. Under the most favourable conditions this part of the process takes about an hour. The contents of the flask are then cooled and diluted with water. They are next transferred to the flask F (Fig. 10),

and to the liquid is added from the tap funnel T a concentrated solution of caustic soda considerably more than would be required to neutralise the original amount of sulphuric acid. The liquid in F is then boiled, and the steam passes through the drop-catching bulb B, which is introduced to prevent the carrying over of minute drops from the boiling alkaline liquid. The ammonia which passes over with the steam is partially dissolved by the water condensed in C, and the whole is finally absorbed in the acid contained in E.

If mercuric sulphate has been employed as a catalyst, it is necessary to add to the liquid in F a small quantity of sodium sulphide along with the caustic soda. If sodium sulphide is not added, the ammoniacal mercury compounds formed from the mercuric salt and ammonia are very slowly decomposed by the excess of alkali, so that the complete distillation of the whole of the ammonia would occupy a very long time. When sodium sulphide is used this reacts at once with these compounds, converting the mercury into insoluble mercuric sulphide and liberating the ammonia.

Estimation of Halogens, Sulphur, Phosphorus, etc.

These elements are frequently estimated by Carius's method, which consists in heating the organic substance with a large excess of concentrated nitric acid in a sealed tube. Complete destruction of the organic compound occurs: chlorine and bromine appear as hydrochloric and hydrobromic acids (or rather as the corresponding silver salts, solid silver nitrate being used in conjunction with the nitric acid), sulphur as sulphuric acid, and phosphorus as phosphoric acid. These compounds are then estimated by the usual methods employed in inorganic analysis.

DETERMINATION OF MOLECULAR WEIGHTS.

Vapour Density.

According to Avogadro's principle, expressed quantitatively in terms of the ordinary chemical units, the molecular weight of a gaseous substance is that weight in grams which would be contained in a volume of 22·4 litres at 0° centigrade and 760 mm. pressure. If, therefore, we measure the weight and volume of a quantity of gas under these conditions, we are in a position to calculate its molecular weight. Even if the substance cannot be obtained in the gaseous state under these normal conditions of temperature and pressure, the determination of the molecular weight is still possible if the substance can be vaporised at all, for it is then only necessary to make the reduction of the volume at the temperature and pressure of observation to the volume at 0° and 760 mm. by means of the laws of Boyle and Gay-Lussac.

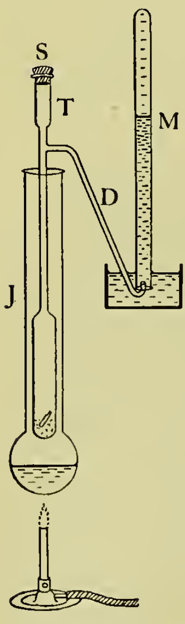


FIG. 11.

Since most of the substances dealt with in organic chemistry are either liquid or solid at the ordinary temperature, it is almost invariably necessary to determine the molecular weights at a temperature considerably above 0°, and several methods have been devised for carrying out the determination with ease and rapidity. The method most frequently adopted by organic chemists is known as **Victor Meyer's method.** The apparatus for it is comparatively simple, and is shown in Fig. 11. It consists of a tube, T, in which the substance is vaporised. This

tube ends in a long bulb, and is provided at the upper portion with a side-tube through which gas can escape after the insertion of the stopper S. Surrounding the tube T is a wider tube, J, which acts as a jacket for keeping the inner tube at a constant temperature by means of a suitable liquid, which is kept boiling in the outer bulb, and whose vapours are made to condense in the lower three-fourths of the tube. The temperature at which the evaporation takes place is the boiling-point of the liquid in J. It is well to choose a liquid the boiling-point of which is well above that of the substance whose vapour density is to be determined. The end of the delivery tube is made to dip under the surface of water, and over it is inverted a gas-measuring tube completely filled with water.

The determination is conducted as follows:—The apparatus being arranged as shown in the figure, the liquid in J is boiled steadily, so as to heat the bulb and part of the stem of T. The stopper S meanwhile is only loosely placed in the neck of T. When the distribution of temperature has become constant, a small bottle containing a weighed quantity of the substance whose vapour density is to be determined is dropped into the bulb of T, the stopper S being removed for an instant to permit of this, and then at once replaced tightly. The substance soon gets heated above its boiling-point, and vaporised from the small bottle. The vapour remains in the hot bulb of T, but displaces air through the side-tube, this air passing into a measuring tube, M. After a few minutes the substance is completely vaporised, and no more air passes out of the side-tube. The distribution of temperature at the end of the experiment is the same as at the beginning, so that if the pressure, volume, and temperature of the air in the measuring vessel are noted, these may be assumed to have the same values as would be given by the weighed quantity of substance as vapour under the same conditions.

The following example shows the method of calculation. A quantity of a liquid weighing 0·1104 gram yielded 23·2 c.c. of air, measured over water at 18° and 772 mm. pressure. This value of 772 mm. is made up of the pressure of the air, and the pressure of the water vapour with which it is mixed. The magnitude of the latter may be ascertained from a table of the

vapour pressures of water. From such a table it appears that at 18° water has a vapour pressure of 15 mm., so that the pressure of the gas is not 772 mm., but $772-15=757$. Reducing the volume of air to normal pressure and temperature, we obtain

$$\frac{23 \cdot 2 \times 273 \times 757}{291 \times 760} = 21 \cdot 7 \text{ c.c.}$$

We have thus found that 0·1104 of the substance would occupy 21·7 c.c. at 0° and 760 mm., and have now only to ascertain the weight which would occupy 22·4 litres under the same conditions. This weight is

$$\frac{0 \cdot 1104 \times 22{,}400}{21 \cdot 7} = 114.$$

The molecular weight of the substance, then, as found in this experiment is 114.

Any molecular weight so obtained is only approximate, since the error in Victor Meyer's determination under ordinary conditions may amount to as much as 5 per cent. For the purpose of determining the formula, however, this accuracy is sufficient. The substance here actually used was known to have the empirical formula $CHCl_3$, which would give the formula weight 119·5. This weight is sufficiently close to the value 114 obtained by experiment to show conclusively that the empirical formula weight and the molecular weight are in this instance identical, and that the molecular formula of the substance is $CHCl_3$.

Freezing-point Depression.

The method of vapour density for determining the molecular weight of substances is plainly available only when these are volatile without decomposition, and cannot therefore be employed, say, in the case of a substance like sugar, which decomposes on heating to a temperature far beneath that at which it would vaporise. It is possible, however, to determine the molecular weight of such non-volatile substances by observing the behaviour of their solutions, various properties of which

may be utilised in determining the molecular weight of the dissolved substance. The property most frequently made use of in organic chemistry is the **freezing-point.** It has long been known that the freezing-point of aqueous solutions is lower than the freezing-point of pure water, and with dilute solutions the difference between the freezing-point and that of pure water—that is, the **freezing-point depression**—is proportional to the concentration of the solution. Thus, a 2 per cent. sugar solution freezes twice as far below the freezing-point of water as a 1 per cent. solution.

When aqueous solutions of different substances are compared, it is found in general that those solutions which contain dissolved in them quantities of the substances which are proportional to their molecular weights have the same freezing-point; that is, the lowering of the freezing-point is the same when the solutions contain equal numbers of the dissolved molecules. Thus, if a substance had half the molecular weight of sugar, a 0·5 per cent. solution of it would show the same depression of the freezing-point as a 1 per cent. solution of sugar, for then equal volumes of the two solutions would contain the same number of dissolved molecules. Experiment shows that solutions of various substances which contain 1 gram molecule of the substance dissolved in a kilogram of water have all approximately the freezing-point of $-1·86°$ C.; that is, the lowering of the freezing-point of these molecular normal solutions is 1·86. If, then, we find that a solution of an unknown substance shows a freezing-point depression of 1·86, we may conclude that it contains 1 gram molecule per litre of water; and if we analyse the solution so as to ascertain the amount of dissolved substance, we can say that the number of grams dissolved in 1 litre of the water gives, at least approximately, the molecular weight of the substance.

This method of determining molecular weights by the freezing-point is frequently spoken of as **Raoult's method**, and is practically carried out in the apparatus sketched in Fig. 12. The tube F contains the liquid the freezing-point of which is to be determined, and through the cork closing the widened upper portion there pass a thermometer and a stirrer, S, which moves freely up and down through a tube in the cork. The side-tube is for the purpose of introducing weighed quantities

of the substance to be dissolved in the liquid contained in F. If the solvent is water, the apparatus must be surrounded by a jacket at a temperature beneath the freezing-point of water. A freezing-mixture of ice, salt, and water is therefore introduced into the wide jar J, and into this the tube F is immersed. In order, however, to prevent direct contact of the water or solution in F with the freezing mixture, a wide test-tube, T, is interposed, the space between this and the inner tube F being empty. The freezing mixture is stirred from time to time by means of a large stirrer provided in the outer jar.

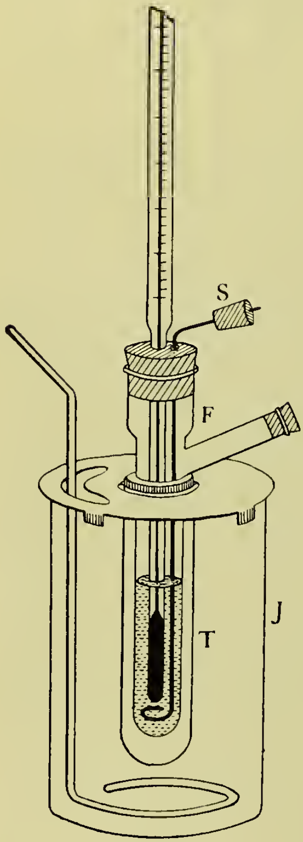


FIG. 12.

To perform the experiment, a weighed or measured portion of the solvent — here water — is placed in F, and the apparatus arranged as in the figure. As the freezing mixture in J has a temperature of from $-5°$ to $-10°$, the water gradually cools until its temperature falls below its freezing-point. After a time ice begins to separate in the tube, and the liquid is then stirred vigorously in order to get good contact between ice and water. The thermometer then registers the freezing-point of water.

A weighed quantity of the substance to be dissolved, say sugar, is then introduced in the form of a pellet through the side-tube. It dissolves in the water, the process of solution being aided by constant stirring. If all the ice which has separated melts during this process of solution, the liquid is allowed to cool further until ice again separates. Once more the liquid is briskly stirred, and the thermometer observed during a few minutes. Generally speaking, a rise of the thermometer is first seen,

and then a slow fall. The maximum temperature which the thermometer registers is accepted as the freezing-point of the solution.

We have now observed two temperatures: first, the freezing-point of the pure water, and second, the freezing-point of the solution. The difference between these is the lowering of the freezing-point, and from this and the concentration of the solution the molecular weight may be calculated.

The method of calculation is simple, as may be seen from the following example. An aqueous solution of ethyl alcohol, containing 8·74 grams of alcohol in 1000 grams of water, gave a freezing-point depression of 0·354°. A gram molecular weight of alcohol dissolved in 1000 grams of water would have given a depression of 1·86°. Such a solution must then contain

$$\frac{8{\cdot}74 \times 1{\cdot}86}{0{\cdot}354} = 45{\cdot}9 \text{ grams,}$$

i.e. the molecular weight of alcohol found in this experiment is 45·9; but the empirical formula of ethyl alcohol is C_2H_6O, which represents 46 grams. We see, then, that in this case also the empirical formula and the molecular formula are identical.

If a salt such as sodium chloride is dissolved in water the freezing-point depression is considerably greater, in dilute solutions nearly twice as great, as that which would be calculated from the simplest formula NaCl. This abnormal result is explained on the assumption that since the aqueous solutions of sodium chloride are good electrolytes, the dissolved salt is largely split up into positive and negative ions, $Na^{\cdot}$ and Cl', each of which acts as an independent molecule and produces its own effect in depressing the freezing-point. Where electrolytes are concerned, allowance must always be made for similar ionisation.

Besides water, other solvents are employed for use in determining molecular weights by Raoult's method, for many organic substances are insoluble or very sparingly insoluble in water. The chief of these other solvents are acetic acid and benzene, which freeze at 16·5° and 5·5° respectively. The following table contains the freezing-point constants, that is,

the depression caused by dissolving 1 gram molecule of a substance in 1000 grams of solvent:—

Water	1·86
Acetic acid . . .	3·88
Benzene	4·90

VALENCY AND GRAPHIC FORMULÆ.

According to the atomic theory, the smallest separable particle of any compound—the molecule—is built up of the ultimate particles or atoms of the elements which it contains. On this supposition it is evidently a matter of enquiry how the atoms are arranged in any given case to form the molecule. This question is not always susceptible of a definite answer, but in organic chemistry we have fairly clear ideas of the atomic arrangement in the molecule for the vast majority of compounds. That some determinate arrangement occurs is evident from the fact that we are acquainted with many compounds which have exactly the same composition and molecular weight, but yet possess entirely different properties, both physical and chemical. In view of the identity of composition and molecular weight, the molecules of these substances, which are said to be **isomeric** with each other, must contain the same kinds of atoms, and the same numbers of the various kinds. The only mode, therefore, which we possess of accounting for the great differences in properties is to attribute them to different arrangements of the atoms constituting the different kinds of molecule.

Now when we come to consider these arrangements in detail, we find in the first place that certain regularities appear in the simple compounds of the elements with one another which greatly restrict the total number of compounds. If we consider, for example, those compounds of carbon with one other element which contain only one atom of carbon, we find that the maximum number of these other atoms which exist in the compound with the single atom of carbon never exceeds four. Thus we have the compounds CO, CO_2, CS_2, CH_4, CCl_4. Four, then, would seem to be the maximum number of other atoms with which one atom of carbon can combine.

This number 4 is often spoken of as the maximum **combining capacity,** or **valency,** of the atom of carbon. By similar enquiry we ascertain that the maximum combining capacity or valency of oxygen in ordinary compounds is two, and that the valency of hydrogen is one. Thus we may say that hydrogen is univalent, or monad; oxygen bivalent, or dyad; carbon quadrivalent, or tetrad.

Such valencies may be conveniently indicated in formulæ by means of straight lines attached to the symbols of the atoms, each line indicating a possible combination with another atom: so we may write hydrogen, with its single valency, thus H—; oxygen, with its valency of two, thus —O—; and carbon, with its valency of four, thus $\begin{array}{c} | \\ -\mathrm{C}- \\ | \end{array}$. Such straight lines may further be utilised in the formula of a compound to indicate the mode of attachment of the atoms in a molecule. Thus, in the molecule of hydrogen we have two atoms of hydrogen, each with a single valency. We may consequently write the molecular formula of hydrogen as follows, H— —H, or simply H—H, and indicate thereby that two atoms of hydrogen are directly linked to each other in the molecule. The simple line joining the two atomic symbols is often spoken of as a "bond." It should not, however, be regarded as anything material joining the two atoms. What physical significance it has is probably electrical, but at the outset we should regard it solely as denoting direct union of atoms.

To take another example. In the water molecule we have two atoms of hydrogen and one of oxygen. In order to write its graphic formula by means of which we indicate the arrangement of the atom within the molecule, we make use of the symbols H—, H—, and —O—. The only way in which all the valencies can be paired off, *i.e.* appear as "bonds" joining the atomic symbols, is H——O——H, or simply H—O—H.

Similarly, we may write the formula of methane, CH_4, as

$$\begin{array}{c} \mathrm{H} \\ | \\ \mathrm{H}-\mathrm{C}-\mathrm{H} \\ | \\ \mathrm{H} \end{array}$$

and carbon dioxide may be written as follows :—

$$O{=}C{=}O.$$

This is the only possible formula which makes both oxygen atoms dyad and the carbon atom tetrad.

It is sometimes in exceptional cases impossible to write a graphic formula strictly in accordance with the above principles. Thus carbon monoxide, CO, must be either written as $C{=}O$ with dyad carbon or as $C{\equiv}O$ with tetrad oxygen. Such cases, however, are rare.

The compound methane, CH_4, is the only compound of carbon and hydrogen, or hydrocarbon, containing a single atom of carbon in the molecule. There are three hydrocarbons containing two atoms of carbon in the molecule, namely, ethane, C_2H_6, ethylene, C_2H_4, and acetylene, C_2H_2. Since hydrogen has only one valency, *i.e.* is capable of uniting directly with only one other atom, it follows that in these three compounds the two carbon atoms must be directly united to each other. Their graphic formula must, therefore, contain the following arrangement of the carbon atoms :—

$$\begin{array}{ccccc} & | & & | & \\ - & C & - & C & - \\ & | & & | & \end{array}$$

This formula contains six valencies still unsatisfied.

In the molecule of ethane there are six hydrogen atoms, which would exactly satisfy these valencies, so that we may write the formula of ethane as follows :—

$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

In ethylene, with the formula C_2H_4, two valencies must remain unsatisfied, so that we might write the graphic formula either—

$$\begin{array}{ccccccc} & & H & & & & \\ & & | & & | & & \\ H & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & & & \end{array} \qquad \text{or} \qquad \begin{array}{ccccc} & H & & H & \\ & | & & | & \\ - & C & - & C & - \\ & | & & | & \\ & H & & H & \end{array}$$

In the first formula the two unsatisfied valencies are on the same carbon atom; in the second, there is one valency free on each. A study of the properties of ethylene make it beyond doubt that the second formula is the better representation. In general it may be said that blank valencies occur in pairs on adjacent carbon atoms.

A hydrocarbon like ethane, with all its carbon valencies satisfied, is said to be **saturated.** A hydrocarbon like ethylene, with carbon valencies still unsatisfied by combination with other atoms, is said to be **unsaturated.** These terms correspond to a real difference in behaviour. Thus ethane, being saturated, will not directly combine with other substances by addition. Ethylene, on the other hand, being unsaturated, can be made to combine with other substances, thus:—

$$\begin{array}{lcl} C_2H_4 + H_2 & = & C_2H_6 \\ C_2H_4 + Cl_2 & = & C_2H_4Cl_2 \\ C_2H_4 + Br_2 & = & C_2H_4Br_2 \end{array}$$

The unsaturated ethylene, by combining with hydrogen, chlorine, or bromine, gives the following saturated compounds:—

$$\begin{array}{ccc} \begin{array}{c} \text{H}\quad\text{H} \\ |\quad\;\; | \\ \text{H—C—C—H} \\ |\quad\;\; | \\ \text{H}\quad\text{H} \end{array} & \begin{array}{c} \text{Cl}\quad\text{Cl} \\ |\quad\;\; | \\ \text{H—C—C—H} \\ |\quad\;\; | \\ \text{H}\quad\text{H} \end{array} & \begin{array}{c} \text{Br}\quad\text{Br} \\ |\quad\;\; | \\ \text{H—C—C—H} \\ |\quad\;\; | \\ \text{H}\quad\text{H} \end{array} \\ \text{Ethane} & \text{Ethylene chloride} & \text{Ethylene bromide} \end{array}$$

It may be noted that the halogen atoms (chlorine, bromine, and iodine) in organic compounds are treated as univalent, like hydrogen.

It has become customary to write the formula of ethylene and similar unsaturated substances, not with blank valencies, but with "double bonds," as follows:—

$$\begin{array}{c} \text{H—C=C—H} \\ |\quad\;\; | \\ \text{H}\quad\text{H} \end{array}$$

The double bond between carbon atoms merely indicates a want of complete saturation, and not any closer union of the atoms.

Acetylene is still less saturated than ethylene, and its formula may be written in either of the following ways, the method of writing with a "triple bond" being the more common:—

$$\begin{array}{ccccccc} & & | & & | & & \\ H & — & C & — & C & — & H \\ & & | & & | & & \end{array} \qquad H—C\equiv C—H$$

Instead of lines being used to represent the bonds, dots may be conveniently employed in the same sense, especially in contracted formulæ. Thus we may write methane as—

$$\begin{array}{c} H \\ \cdot \\ H.C.H, \\ \cdot \\ H \end{array} \text{ and ethane as } \begin{array}{c} H\ H \\ \cdot\ \ \cdot \\ H.C.C.H \\ \cdot\ \ \cdot \\ H\ H \end{array}$$

or contracted, as $CH_3.CH_3$, in which we look upon it as two univalent CH_3 groups joined directly together. Ethylene may similarly be written—

$$\begin{array}{c} H.C:C.H \\ \cdot\ \ \cdot \\ H\ H \end{array} \quad \text{or} \quad CH_2:CH_2$$

and acetylene as $H.C\vdots C.H$ or $CH\vdots CH$.

Graphic Formulæ of Inorganic Compounds.

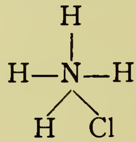
When we consider compounds of other elements than carbon, oxygen, and hydrogen, we find that we are no longer in a position to write their graphic formulæ with the same certainty as exists in the case of organic compounds. This is due to the circumstance that these other elements have a variable valency.

If we consider the element **nitrogen**, we see that in ammonia it must be triad, since hydrogen is never other than monad; and we may write the graphic formula of ammonia thus—

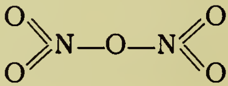
$$\begin{array}{ccccc} & & H & & \\ & & | & & \\ H & — & N & — & H \end{array}$$

This compound, however, is in a sense unsaturated. It combines at once with acids to form ammonium salts, say with hydro-

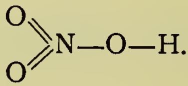
chloric acid to form ammonium chloride, which is more readily represented graphically by making the nitrogen pentad, thus—



In the fully oxidised compounds of nitrogen the element may also be conveniently assumed to be pentad. Thus we write nitrogen pentoxide—



and nitric acid—



Here it will be observed that the replaceable hydrogen is part of the hydroxyl group OH.

In nitrous acid derived from the trioxide

$$O{=}N{-}O{-}N{=}O,$$

the nitrogen is generally conceived as triad, and the graphic formula of nitrous acid is written—

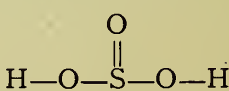
$$O{=}N{-}O{-}H.$$

Sulphur may be dyad, tetrad, or hexad. In sulphuretted hydrogen it is dyad, thus—

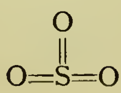
$$H{-}S{-}H.$$

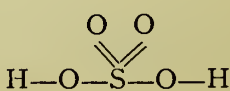
In sulphur dioxide and sulphurous acid it is looked upon as tetrad, thus—

$$O{=}S{=}O$$

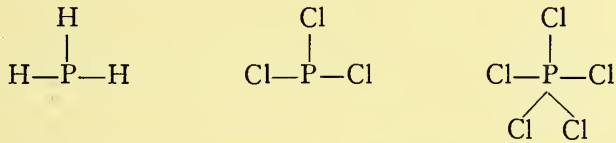


In sulphur trioxide and sulphuric acid it is hexad, thus—

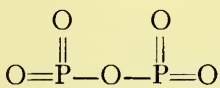




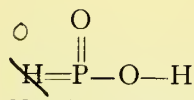
Phosphorus is like nitrogen, either triad or pentad. For example, we have—



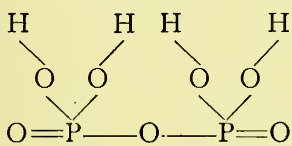
In the fully oxidised phosphoric acid and its derivatives it is pentad, thus—



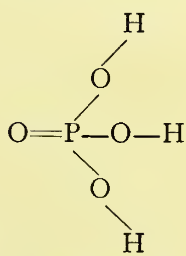
Phosphorus pentoxide



Metaphosphoric acid



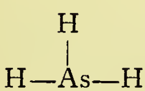
Pyrophosphoric acid



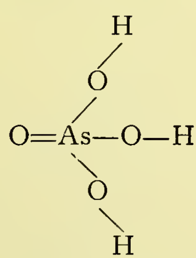
Orthophosphoric acid

It should be particularly noted that the replaceable hydrogen of the strong oxygen acids is always part of the group —OH or hydroxyl.

Arsenic, like nitrogen and phosphorus, is triad or pentad, *e.g.*—



Arsine



Arsenic acid

Organic derivatives of many of the above compounds are of frequent occurrence, and in them the elements are represented as retaining the valencies here given.

DISTILLATION OF WOOD.

When wood is heated in absence of air the residue is known as wood charcoal. In former times this was the chief product aimed at in the heating of wood. At present, however, the production of wood charcoal is accompanied by the formation of other products which have considerable commercial value and are important as starting-points for the production of many organic compounds.

Green wood contains a very large proportion of moisture, which may amount to considerably more than half the weight of the wood. When the wood dries in air the bulk of this moisture evaporates, but even in dried wood as much as 15 to 20 per cent. of moisture remains. When such dry wood is exposed to a gradually increasing temperature the remaining moisture is driven off; but when the temperature reaches 150°, a process of decomposition of the solid material of the wood sets in, with production of water and a great many different organic compounds. These compounds are derived almost entirely from cellulose, $C_6H_{10}O_5$, and similar substances of which the dry wood consists. The nature and proportions of the products of decomposition depend upon the mode of heating. If the temperature is raised rapidly from 150°, the quantity of charcoal obtained, for instance, is much greater than when the temperature is raised slowly. Generally speaking, the operation may take from three to six hours, and is conducted in retorts to which the air has no access. At the end of the distillation, wood charcoal remains in the retort, and the volatile products appear either in the form of liquid deposited in the water-cooled condenser, or as gases which escape condensation. From 100 parts of wood the follow-

ing quantities of the various products are, roughly speaking, obtained :—

Charcoal	25 parts
Aqueous distillate	45 „
Wood tar	5 „
Gas	25 „

These proportions are, of course, liable to great variation, according to the nature of the wood and the mode of heating.

The **charcoal** consists almost entirely of the element carbon, mixed, however, with a certain amount of still undecomposed carbon compounds and the inorganic constituents of the wood, chiefly in the form of potassium carbonate.

Wood tar is a thick, black liquid, nearly insoluble in water, which, on account of its antiseptic properties, is largely used as a preservative for wood and as a source of antiseptic substances for surgical purposes. If pine wood or other coniferous wood is distilled, the tarry product is known as **Stockholm tar,** which is the official tar of the Pharmacopœia.

The gas given off during the distillation of wood consists chiefly of hydrogen, methane, and oxides of carbon. It has no value for illuminating purposes, but is useful as a gaseous fuel for heating the retorts in which the wood is distilled.

The aqueous distillate consists for the most part of water, but contains roughly the following proportions of soluble organic substances derived from 100 parts of the original wood :—

Acetic acid, $CH_3.COOH$	5 parts
Acetone, $CH_3.CO.CH_3$	0·2 „
Methyl alcohol, $CH_3.OH$	0·7 „

This solution is of a dark brown colour, and is known as **pyroligneous acid.** From it, acetic acid and methyl alcohol are commercially prepared. The boiling-point of methyl alcohol is 66°, that of acetone is 56°, whilst acetic acid and water boil over together between 100° and 120°, depending on the proportions of which they are present. When the pyroligneous acid is distilled, therefore, and the receivers are changed at 100°, the greater part of the methyl alcohol and

acetone are separated from the acetic acid. In order to make the separation more nearly perfect, it is customary to pass the vapours through hot milk of lime, which combines with the acetic acid, forming calcium acetate, and allows the other substances to pass on unchanged as vapours, which are then condensed.

Methyl Alcohol, CH_3OH.

The first distillate is known as **wood naphtha** or **wood spirit**. It is used for the purpose of methylating rectified spirit and rendering it unpalatable. It is generally somewhat coloured, and on diluting with water becomes turbid, owing to the separation of oily substances which pass over as vapour along with it. To prepare pure methyl alcohol, it is diluted with water until these oily substances separate. They collect on standing as a separate layer which may afterwards be removed. In order to eliminate the last traces of acid, the liquid is mixed with a little lime and redistilled in a rectifying still. The methyl alcohol still possesses a disagreeable odour and a slight colour, to get rid of which it is filtered through charcoal and again distilled over lime. It now contains very little water, but is not yet free from acetone. For many purposes the presence of this latter substance is unimportant. If methyl alcohol free from acetone is required, it may be obtained by treating the mixture with anhydrous calcium chloride, which combines with the methyl alcohol to form the solid compound $CaCl_2,4CH_3OH$, which is stable at 100°. The methyl alcohol in this compound resembles the water of crystallisation in the hydrate $CaCl_2,6H_2O$. By gently warming this alcoholate the low-boiling acetone may be expelled. On treatment now with water the alcoholate is decomposed, and the methyl alcohol may be separated from the salt and water by repeated distillation, finally over quicklime.

Methyl alcohol is a colourless liquid, and has a specific gravity of about 0·8. It boils at 66°, and has a faint, not unpleasant odour and a burning taste. It burns with a non-luminous flame, and mixes with water in all proportions, a slight contraction and production of heat attending the mixing.

On a large scale it is used in the impure state as a solvent, and in the manufacture of many organic dyes. Its chief medicinal use is in the preparation of the gaseous disinfectant formaldehyde, by means of its slow combustion.

In many respects it resembles water in its chemical properties. As we have just seen, it forms alcoholates with certain salts corresponding to the hydrates. It is readily attacked by sodium, which dissolves in it with evolution of hydrogen, according to the equation—

$$2Na + 2CH_3OH = H_2 + 2NaOCH_3.$$

The substance $NaOCH_3$, *sodium methoxide*, is a white solid analogous to sodium hydroxide. Methyl alcohol acts as a solvent for many salts, and for substances which are soluble in water; and it may be said in general that those substances which, dissolved in water, yield electrolytic solutions give also electrolytic solutions when dissolved in methyl alcohol.

METHANE AND ITS DERIVATIVES.

The **hydrocarbons** are those compounds which consist of carbon and hydrogen only. For purposes of classification and nomenclature it is customary in organic chemistry to conceive the various compounds as being derived from saturated hydrocarbons containing an equal number of atoms of carbon by the substitution of other elements, or groups of elements, for the hydrogen which these hydrocarbons contain. There is only one hydrocarbon, namely methane, CH_4, which contains a single atom of carbon, and so all other compounds containing a single atom of carbon may be referred to methane as the parent substance.

Methane, CH_4.

Methane, or marsh-gas, occurs in nature where vegetable matter is decaying, or has decayed, in absence of air. Thus it is found in the bubbles of gas rising from decaying vegetation in marshes, and is also found in cavities in coal-mines, where it has probably been produced from similar decomposition of vegetable matter. When these cavities are broken into by the miner the gas escapes into the galleries of the pit, and on account of its forming an explosive mixture with air, is known as **fire-damp.** Methane is also found in large quantity in the natural gas which issues from the ground in regions where petroleum is found; and it is also one of the chief constituents of coal-gas, which contains usually 30 to 40 per cent. of methane.

Methane is conveniently prepared in the laboratory by heating anhydrous sodium acetate with a large excess of soda-lime to a high temperature. The equation for this action is—

$$\underset{\text{Sodium acetate}}{CH_3.COONa} + NaOH = \underset{\text{Methane}}{CH_4} + Na_2CO_3.$$

Prepared in this way methane is not quite pure, but contains

small quantities of other hydrocarbons and of hydrogen. Methane is a colourless inodorous gas which is very sparingly soluble in water, and cannot be condensed to the liquid state at the ordinary temperature. It burns with a feebly luminous flame, the complete combustion being expressed by the equation—

$$\underset{1\text{ vol.}}{CH_4} + \underset{2\text{ vols.}}{2O_2} = \underset{1\text{ vol.}}{CO_2} + 2H_2O.$$

It is not attacked by chlorine in the dark, but if exposed to diffused light it is slowly acted upon by the chlorine, with ultimate production of carbon tetrachloride—

$$CH_4 + 4Cl_2 = CCl_4 + 4HCl.$$

If the mixture of methane and chlorine is exposed to bright sunlight, or is fired by means of a taper, the reaction which takes place is different, the chlorine combining with the hydrogen only, and carbon being deposited—

$$CH_4 + 2Cl_2 = C + 4HCl.$$

Other actions of chlorine on methane will be considered in the sequel.

It should be noticed that, although saturated hydrocarbons may be regarded as the parent substances of other carbon compounds for purposes of classification, they are practically never used as sources of these compounds, owing principally to the difficulty experienced in attacking them by the ordinary chemical reagents. Thus methane, although it occurs in quantity in nature and is one of the principal gaseous products of the dry distillation of coal, is never used for the preparation of other compounds of carbon containing a single atom of carbon. Methyl alcohol, on the other hand, which is a partially oxidised form of methane, can be used as a starting-point for the preparation of other carbon compounds, owing to its superior activity—that is, to the comparative ease with which it is attacked by certain chemical reagents.

Oxygen Derivatives of Methane.

As it is of great importance that the relationship between the hydrocarbons and their oxidation products should be clearly

grasped, some consideration will now be given to the complete series of the oxidation products of methane. If we compare the formula of methane, CH_4, with that of methyl alcohol, CH_3OH, we see that methyl alcohol may be regarded as being derived from methane by the substitution of the univalent hydroxyl group OH for the univalent atom hydrogen. It is evident that the process of substituting the hydroxyl group for the hydrogen atom may be repeated four times in the case of methane, so that there are four successive stages in the oxidation by substitution of the hydroxyl group for hydrogen. This form of oxidation is frequently spoken of as hydroxylation. The following table gives the graphic formulæ of the successive hydroxyl products of methane:—

$$\begin{matrix} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{OH} \\ & | & \\ & \mathrm{H} & \end{matrix} \qquad \text{Methyl alcohol}$$

$$\begin{matrix} & \mathrm{OH} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{OH} & \end{matrix} = H_2O + \begin{matrix} & \mathrm{O} & \\ & \| & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \end{matrix} \qquad \text{Formaldehyde}$$

$$\begin{matrix} & \mathrm{OH} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{OH} \\ & | & \\ & \mathrm{OH} & \end{matrix} = H_2O + \begin{matrix} & \mathrm{O} & \\ & \| & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{OH} \end{matrix} \qquad \text{Formic acid}$$

$$\begin{matrix} & \mathrm{OH} & \\ & | & \\ \mathrm{HO}- & \mathrm{C} & -\mathrm{OH} \\ & | & \\ & \mathrm{OH} & \end{matrix} = H_2O + \begin{matrix} & \mathrm{O} & \\ & \| & \\ \mathrm{HO}- & \mathrm{C} & -\mathrm{OH} \end{matrix} \qquad \text{Carbonic acid}$$

$$\text{or} \quad = 2H_2O + \begin{matrix} \mathrm{O} & \\ \| & \\ \mathrm{C} & =\mathrm{O} \end{matrix} \qquad \text{Carbonic anhydride}$$

The first oxidation product is, as we see, **methyl alcohol.** This substance is a particular example of a very large class of organic substances. They all contain the group hydroxyl OH, attached to a carbon atom which is not otherwise oxidised, and are termed as a class, the alcohols. Alcohols which, like

methyl alcohol, contain a univalent group, CH_2OH, are called primary alcohols.

The next stage in the process of hydroxylation is that corresponding to **formaldehyde.** In the original hydroxylated product there are two hydroxyl groups. Now it is a general rule of organic chemistry that, when two hydroxyl groups are attached to one and the same carbon atom, they readily lose the elements of water, and their place is taken by a single oxygen atom. It will be seen that this process is closely analogous to what sometimes happens in organic chemistry. Calcium hydroxide, $Ca(OH)_2$, when heated to a sufficiently high temperature, loses water and is converted into calcium oxide, CaO, two hydroxyl groups having jointly lost water between them and been replaced by a dyad oxygen atom. If we write this graphically, we see that it is precisely analogous to the loss of water by the doubly hydroxylated methane—

$$\mathrm{Ca}\begin{matrix}\diagup \mathrm{OH}\\ \diagdown \mathrm{OH}\end{matrix} \rightleftharpoons \mathrm{Ca{=}O} + \mathrm{H{-}OH}.$$

It is true that in the case of calcium hydroxide a red heat is required to effect the decompositions, but with some other hydroxides—for example, mercuric hydroxide—this is not the case. Even at the ordinary temperature, mercuric hydroxide loses water and is converted into mercuric oxide, HgO.

As we shall see later, formaldehyde when dissolved in water almost certainly exists to some extent at least as a hydrated form, $CH_2(OH)_2$, although when we attempt to isolate this substance we fail, owing to the ease with which it loses the elements of water. These actions may be expressed by the reversible equation—

$$\begin{matrix}\mathrm{H}\diagdown\\ \mathrm{H}\diagup\end{matrix}\mathrm{C}\begin{matrix}\diagup \mathrm{OH}\\ \diagdown \mathrm{OH}\end{matrix} \rightleftharpoons \begin{matrix}\mathrm{H}\diagdown\\ \mathrm{H}\diagup\end{matrix}\mathrm{C{=}O} + \mathrm{HOH}.$$

Just as the group CH_2OH is characteristic of the whole class of primary alcohols, so the group $CO.H$ is characteristic of the whole class of **aldehydes.** These aldehydes may be, and for the most part are, actually prepared from primary alcohols by a process of oxidation. Formaldehyde, for example, is usually

prepared by the oxidation of methyl alcohol. It is also possible, on the other hand, by the use of reducing agents, to reduce the aldehydes to primary alcohols, the general scheme for the reduction being as follows :—

$$R.CO.H + 2(H) = R.CH_2.OH.$$

In this equation R represents a univalent organic radical.

The next stage in the hydroxylation of methane is that of **formic acid.** The original hydroxylated product, $CH(OH)_3$, sometimes known as ortho-formic acid, contains three hydroxyl groups attached to a single atom of carbon. It, therefore, like the aldehydes, rapidly loses water between two of them, and the monad group $C(OH)_3$ becomes the monad group COOH. This group, which is termed the **carboxyl group**, is the characteristic group of organic acids, the hydrogen of the group readily appearing as an ion in aqueous solution and being replaceable by metals. The organic carboxylic acids are not only formally oxidation products of the aldehydes, but may be prepared from them by the use of appropriate oxidising agents. The aldehydes, in fact, have such a tendency to become further oxidised to acids that they, in general, behave as mild reducing agents, and some of them are even capable of taking up oxygen from the air and thus becoming converted into acids. Generally speaking, the carboxylic acid is the final stage in the oxidation of the carbon atom, but in the special case of methane, in which the carbon atom, unlike those of all other hydrocarbons, is not attached to any other carbon atom, the hydroxylation may be still carried one stage further. The complete hydroxylation product is $C(OH)_4$. This substance with four hydroxyl groups is capable of losing two molecules of water, one from each of the two pairs of hydroxyl groups, the products of dehydration being carbonic acid, H_2CO_3, and carbon dioxide, CO_2. If we refer to the formula of formic acid, H.CO.OH, we see that it still contains the characteristic aldehyde group H.CO or CO.H, and is thus theoretically capable of hydroxylation to an acid.

Carbonic acid cannot be isolated, owing to the readiness with which it loses one molecule of water from the two hydroxyl groups and becomes converted into the anhydride CO_2. It

certainly exists, however, to some extent in aqueous solution, for the solution of carbon dioxide in water has all the characteristic reactions of a weak acid. It is even possible that to a small extent some of the fully hydroxylated form, $C(OH)_4$, ortho-carbonic acid, exists. It should be noted that by passing from formic acid to carbonic acid we pass from a monobasic to a dibasic acid, the aldehyde group HCO of formic acid, in which the hydrogen is not replaceable by metal, becoming the acid group HO.CO, in which the hydrogen is so replaceable.

Formaldehyde, H_2CO.

Formaldehyde is, as has been stated, generally prepared by the oxidation of methyl alcohol. When methyl alcohol burns in air in the ordinary way, it of course burns to carbon dioxide and water; but if the supply of air is limited, then combustion takes place with the production of formaldehyde, according to the equation—

$$2CH_3.OH + O_2 = 2H.CO.H + 2H_2O.$$

The oxidation is usually carried out by passing air through methyl alcohol and then over heated copper or heated platinum, generally in the form of platinised asbestos. The methyl alcohol vapour with which the air is charged is oxidised on the surface of the metal to formaldehyde. This oxidation by means of the catalytic action of the metal may be readily shown by lowering a heated spiral of platinum wire into a beaker containing some warm methyl alcohol. If the wire is lowered to a position where the methyl alcohol vapour and air are in approximately the right proportions, the wire will continue to glow indefinitely, without igniting the methyl alcohol vapour, and the pungent odour of formaldehyde will at once be perceived. The wire remains hot owing to the heat liberated by the combustion of the methyl alcohol on its surface. If the apparatus containing the heated copper or platinised asbestos is connected with a properly cooled condenser, the water and formaldehyde, together with a certain quantity of methyl alcohol, condense and form a solution which contains about one-third of its weight of formaldehyde.

Formaldehyde may also be obtained by heating calcium formate, the reaction being expressed by the equation—

$$\underset{\text{Calcium formate}}{Ca(CO_2H)_2} = \underset{\text{Calcium carbonate}}{CaCO_3} + \underset{\text{Formaldehyde}}{H.CO.H.}$$

This action shows the relationship of a formate to carbonic acid on the one hand, and formaldehyde on the other. The formate, as we see, is partly oxidised to carbonate and partly reduced to formaldehyde.

Formaldehyde when pure is a gas which liquefies at a temperature of about $-20°$. It has a characteristic, penetrating odour, and is largely used as a gaseous disinfectant. It is very soluble in water, and a solution of it containing about 40 per cent. of formaldehyde is known as **formalin** or **formol.** This solution, when diluted, is useful for sterilising surgical instruments, etc., for hardening tissues, and as a preservative for anatomical and other museum specimens.

Formaldehyde, in aqueous solution, is probably to a very large extent in the state of the hydrate $H_2C(OH)_2$, for in dilute solution it shows no tendency to polymerisation, whilst in the anhydrous state it polymerises readily. By polymerisation we mean the phenomenon analogous to that displayed by nitrogen peroxide where two molecules join together to form a more complex molecule, thus—

$$2NO_2 \rightleftharpoons N_2O_4.$$

Similarly to this, formaldehyde in the liquid state or in concentrated solution, especially at a high temperature, polymerises with formation of one or other of two substances. The polymerisation is represented by the equations—

$$2H_2CO \rightleftharpoons (H_2CO)_2 \quad \text{Paraformaldehyde}$$
$$3H_2CO \rightleftharpoons (H_2CO)_3 \quad \text{Trioxymethylene}$$

These substances, **paraformaldehyde** and **trioxymethylene**, are solids, and when heated regenerate formaldehyde according to equations which are the reverse of those just given. Paraformaldehyde is largely used as a source of formaldehyde for the purpose of disinfecting rooms, clothing, etc.

When an aqueous solution of formaldehyde is mixed with calcium or magnesium hydroxide, another kind of polymerisa-

tion takes place, with production of substances which have all properties of sugars. This form of polymerisation may be represented as follows :—

$$6H_2CO = C_6H_{12}O_6.$$

It is possible that the formation of sugar and other carbohydrates in plants is due to a similar polymerisation of formaldehyde.

Ammonia reacts with formaldehyde, according to the equation,

$$6H_2CO + 4NH_3 = (H_2C)_6N_4 + 6H_2O,$$

to produce the solid substance hexamethylene-tetramine, $(H_2C)_6N_4$, which is used, under the name of **urotropine,** as a diuretic.

Formaldehyde acts as a reducing agent, reducing, for example, an ammoniacal solution of a silver salt to metallic silver. It owes its reducing properties to the presence of the aldehyde group CO . H.

Formic Acid, H . COOH.

Formic acid is found in small quantity in nature, chiefly in the stinging parts of plants and animals. It may be obtained from such parts by macerating them with water and distilling, the distillate being a weak solution of formic acid.

It may be prepared in the laboratory by heating oxalic acid with glycerol. The actions which occur are somewhat complicated, but the final result is that the oxalic acid breaks up into carbon dioxide and formic acid according to the equation—

$$\underset{\text{Oxalic acid}}{H_2C_2O_4} = \underset{\text{Formic acid}}{H.COOH} + CO_2.$$

This reaction may be compared with the decomposition of oxalic acid by means of concentrated sulphuric acid, which occurs according to the equation—

$$H_2C_2O_4 = H_2O + CO + CO_2.$$

It will be noticed that in this reaction carbon monoxide and water are obtained instead of formic acid. This would suggest that carbon monoxide is in a sense an anhydride of formic

acid, a view which is confirmed by the fact that carbon monoxide may be prepared by dehydrating formic acid by means of concentrated sulphuric acid—

$$H.COOH = H_2O + CO.$$

Although carbon monoxide is thus, as it were, an anhydride of formic acid, it cannot be made to unite with water to produce formic acid, and it is only with difficulty that it may be brought to unite with alkalies to produce formates. At the ordinary temperature a solution of caustic alkali which dissolves carbon dioxide readily with formation of carbonate has no action upon carbon monoxide. If, however, a very concentrated solution of caustic potash is brought into contact with carbon monoxide as 100°, it slowly absorbs the gas to produce potassium formate—

$$CO + KOH = H.COOK.$$

Formates are now prepared by a method analogous to this. Carbon monoxide is passed over heated soda-lime. It unites freely with the alkali contained in the porous material, with production of formate.

From formates prepared by such methods formic acid may be obtained by heating with dilute sulphuric acid. An aqueous solution of formic acid distils over. A concentrated formic acid may be prepared by heating together sodium formate and sodium hydrogen sulphate in a partial vacuum—

$$H.COONa + NaHSO_4 = Na_2SO_4 + H.COOH.$$

Although formic acid contains two hydrogen atoms in the molecule, only one of these is replaceable by hydrogen, so that it acts as a monobasic acid. It is a considerably stronger acid than acetic acid.

Formic acid is, at the ordinary temperature, a liquid which solidifies when cooled with ice, the melting-point of the pure substance being 8°. The pure acid boils at 101°. The concentrated acid has a strong irritating action on the skin, and has a pungent odour somewhat resembling that of sulphur dioxide.

When heated with concentrated sulphuric acid it breaks up,

as we have seen, into carbon monoxide and water, but when heated alone in closed vessels, decomposition occurs according to the following equation :—

$$H.COOH = CO_2 + H_2,$$

carbon dioxide and hydrogen being formed.

Formic acid possesses reducing properties, being readily oxidised by oxidising agents to carbon dioxide and water—

$$H.COOH + (O) = CO_2 + H_2O.$$

It may be distinguished from acetic acid, which it otherwise closely resembles in its tests, by these reducing properties. Thus, for example, a formate added to an ammoniacal solution of a silver salt reduces the silver compound with precipitation of metallic silver. These reducing properties it owes to the presence of the aldehyde group, since its formula may be written HO¦CO.H, as well as H¦CO.OH.

CHLORINE DERIVATIVES OF METHANE.

In what precedes, we have studied the hydroxylation of methane. We now take up the chlorination of the same hydrocarbon, in order to establish the important relationships which exist between the chlorine derivatives and the hydroxyl derivatives in organic chemistry. Chlorine in its general character is what we term an oxidising agent. We might, therefore, expect that the products of its action on the hydrocarbons such as methane would be in some sense oxidation products of methane. Now we have seen (p. 35) that when chlorine and methane are exploded together, the chlorine takes the hydrogen and the carbon separates out as the element, according to the equation—

$$CH_4 + 2Cl_2 = C + 4HCl.$$

Since the chlorine has here removed hydrogen from the carbon it may be said, according to the wider definition of oxidation, to have oxidised the carbon. When a mixture of methane and chlorine is exposed at the ordinary temperature to sunlight, the chlorine replaces the hydrogen of the methane in a series

of reactions which may be represented by the following equations:—

$$\begin{array}{llll} CH_4 + Cl_2 = HCl + CH_3Cl & \text{Methyl chloride} \\ CH_3Cl + Cl_2 = HCl + CH_2Cl_2 & \text{Methylene chloride} \\ CH_2Cl_2 + Cl_2 = HCl + CHCl_3 & \text{Chloroform} \\ CHCl_3 + Cl_2 = HCl + CCl_4 & \text{Carbon tetrachloride} \end{array}$$

Here the chlorine is said to act by substitution, since it not only removes hydrogen to form hydrochloric acid as before, but an equal quantity replaces the hydrogen by combining with the carbon, so that in the end the methane is not only oxidised to carbon itself, but by the action of the double quantity of chlorine to carbon tetrachloride.

That the various chlorine derivatives of methane may in reality be regarded as oxidation products, is evident when we consider their relations to the corresponding products of hydroxylation. If methyl chloride is heated in a closed vessel with water, it reacts with the water according to the following equation:—

$$CH_3Cl + HOH = HCl + CH_3OH.$$

Here methyl alcohol is produced directly by the action of water and methyl chloride. Now, since water is neither an oxidising agent nor a reducing agent, it is reasonable to regard the methyl chloride from which the methyl alcohol is derived as being at the same stage of oxidation as methyl alcohol itself. This action of water is often spoken of as **hydrolysis**, though the term is here used in a somewhat different sense from that in which we have previously employed it in connection with salts. In salt-hydrolysis we have the splitting up of a salt into acid and base by means of water. In hydrolysis as here used, we have the splitting up of the compound, not into an acid and base, but into an acid and an alcohol. But bases and alcohols have this in common, that they both contain the hydroxyl group. If we compare the hydrolysis of ammonium chloride, which is a true type of salt-hydrolysis, although it only occurs to a very limited extent, with that of methyl chloride, we see that the analogy is very close—

$$NH_4Cl + HOH \rightleftharpoons NH_4OH + HCl.$$
$$CH_3Cl + HOH \rightleftharpoons CH_3OH + HCl.$$

One characteristic of salt-hydrolysis is, that it is reversible. The same holds true of organic hydrolysis. If we pass hydrochloric acid gas into methyl alcohol, a reaction takes place which is the reverse of hydrolysis, and formally corresponds to the neutralisation of the base by the acid.

One point in which organic reactions very often differ from the reactions between inorganic substances is the slowness with which they take place. Thus, while salt-hydrolysis in aqueous solution takes place almost instantaneously, the hydrolysis of a substance like methyl chloride only occurs very slowly at the ordinary temperature. It is found that if the hydroxide of a metal is used instead of water the decomposition of the chloride takes place much more readily, a chloride of the metal being formed instead of hydrochloric acid. For example, when methyl chloride is acted upon by caustic potash, methyl alcohol and potassium chloride are formed according to the equation—

$$CH_3Cl + KOH = CH_3OH + KCl.$$

This action is not, strictly speaking, a hydrolysis or a splitting by means of water, but for convenience it is very often spoken of as hydrolysis by means of alkali. Since substances like methyl chloride are generally very sparingly soluble in water, an alcoholic solution of the alkaline hydroxide is often employed instead of an aqueous solution, for most organic substances are soluble in alcohol. We commonly say then, in such a case, that the methyl chloride is hydrolysed by means of alcoholic potash.

When methylene chloride is hydrolysed with alcoholic potash it gives rise to formaldehyde, according to the equation—

$$CH_2Cl_2 + 2KOH = H.CO.H + 2KCl + H_2O.$$

Similarly, chloroform gives rise to a formate, and carbon tetrachloride to a carbonate, the equations being—

$$\begin{array}{llll} CHCl_3 & + 4KOH = H.CO.OK & + 3KCl & + 2H_2O \\ CCl_4 & + 6KOH = K_2CO_3 & + 4KCl & + 3H_2O \end{array}$$

These reactions clearly show the relationship between the corresponding products of oxidation and products of chlorination of methane.

With regard to the general properties of a series of chlorine compounds such as that which we are now studying, it may be noted in the first place that the substitution of chlorine for hydrogen does not greatly affect the solubility of the compounds. Methane is a substance which is very sparingly soluble in water, much more soluble in organic solvents. The chloro-derivatives of methane are similarly very sparingly soluble in water, but soluble enough in alcohol, ether, benzene, and other organic solvents.

Next, it should be noted that when chlorine is substituted for hydrogen the boiling-point of the compound is raised. The following table shows the effect of the substitution of the boiling-points of methane and the chlorine compounds derived from it:—

		B. Pt.
Methane	CH_4	$-164°$
Methyl chloride	CH_3Cl	$-24°$
Methylene chloride	CH_2Cl_2	$+42°$
Chloroform	$CHCl_3$	$61°$
Carbon tetrachloride	CCl_4	$77°$

The chloro-derivatives of hydrocarbons have generally a narcotic or anæsthetic effect, and it will be noted that chloroform, one of the commonest general anæsthetics, occurs amongst the chloro-derivatives of methane.

Methyl Chloride, CH_3Cl.

This substance, as has already been stated, is prepared by the action of hydrochloric acid on methyl alcohol. Since the action produces water and is reversible, it is plain that the presence of unnecessary water should be avoided during the reaction. Hydrochloric acid gas is therefore used instead of a solution of hydrochloric acid; and in order to increase the velocity of the reaction, and partly at least to annul the effect of the water produced, the action is conducted at the boiling-point of the alcohol, and in presence of a considerable quantity of anhydrous zinc chloride, a salt which has a great affinity for water. The methyl alcohol which evaporates is returned to the flask by a reflux condenser (see Fig. 14), and the methyl chloride, which is gaseous at the ordinary temperature, passes

on. It is washed free from alcohol vapour by being passed through water. It is largely used in the production of organic dyes, and is sometimes employed as a local anæsthetic by being sprayed on the part to be affected, which is cooled by the evaporating liquid till it becomes insensible. For this latter purpose liquefied methyl chloride is kept in small steel cylinders resembling those employed for nitrous oxide.

Chloroform, $CHCl_3$.

Chloroform is prepared by heating a mixture of ethyl alcohol, water, slaked lime, and bleaching powder. The actions which take place are of a somewhat complicated nature, and will be explained at a later stage. As chloroform boils at 61°, it distils from the mixture along with a little alcohol and water. It is purified by being washed with water rendered slightly alkaline, in order to neutralise any hydrochloric acid which may have come over along with the vapours. It is then thoroughly beaten up with concentrated sulphuric acid, separated from the acid, washed again with water, separated, dried with calcium chloride, and distilled.

It may be obtained in a state of purity by the action of caustic soda on chloral, according to the equation—

$$\underset{\text{Chloral}}{CCl_3.CO.H} + NaOH = \underset{\text{Chloroform}}{CHCl_3} + \underset{\text{Sodium formate}}{H.CO_2Na.}$$

The chloroform is distilled off, dried, and redistilled as before.

Chloroform is a colourless liquid with a characteristic sweetish odour. It freezes at $-70°$ and boils at 61°. It is half as heavy again as water, in which it is sparingly soluble, 100 parts of water dissolving 0·7 parts of chloroform. It is not inflammable, owing to the large proportions of the incombustible element chlorine, and the small proportion of the combustible elements carbon and hydrogen which it contains.

When chloroform is prepared for use as an anæsthetic it must be carefully purified, and is best kept either in the dark or in bottles of brown- or amber-coloured glass, to prevent the influence of light, which brings about a reaction between chloroform and the oxygen of the air, with production of irritant products, in particular of carbonyl chloride, $COCl_2$. Chloroform is not only used as an anæsthetic by inhalation of

the vapour, but may also be administered internally or applied externally to allay pain. It is sometimes added to solutions of sugar, gum, etc., as a preservative to prevent fermentation. Chloroform is often used as a solvent for fatty and oily substances, and in particular is sometimes employed instead of carbon bisulphide as a solvent for iodine, giving a violet solution like that produced by carbon bisulphide.

The most characteristic test for chloroform is to warm a little with alcoholic potash and a few drops of aniline. A substance named phenyl-carbylamine is produced, according to the equation,

$$CHCl_3 + \underset{\text{Aniline}}{C_6H_5.NH_2} + 3KOH = \underset{\text{Phenyl-carbylamine}}{C_6H_5.NC} + 3KCl + 3H_2O,$$

and is easily recognisable by its unpleasant odour. It is a poisonous substance, so that care must be exercised in using the test.

Carbon Tetrachloride, CCl_4.

Carbon tetrachloride may be prepared by passing chlorine into boiling chloroform in sunlight, or by passing chlorine into carbon disulphide in presence of a little iodine, which acts as a catalytic agent. The equation representing the reaction is—

$$CS_2 + 3Cl_2 = CCl_4 + S_2Cl_2.$$

Carbon tetrachloride is a colourless liquid, which is somewhat heavier than chloroform, and boils at 77°. It is a good solvent for fats and oils, is not inflammable, and has a characteristic, not unpleasant odour. It possesses anæsthetic properties, but is not used in practice.

BROMINE AND IODINE DERIVATIVES OF METHANE.

Bromine acts upon saturated hydrocarbons in the same manner as chlorine, but the action is generally more sluggish and is less influenced by the action of light. The bromine derivatives are, therefore, seldom prepared directly from the saturated hydrocarbons. Iodine is practically without action on the saturated hydrocarbons under any conditions.

With regard to the properties of the bromine and iodine derivatives as compared with those of the chlorine derivatives,

we find in general that the bromine derivatives boil at a higher temperature and are less volatile than chlorine derivatives, and that the iodine derivatives are less volatile still. Many of the bromine and iodine derivatives are solids at the ordinary temperature where the chlorine derivatives are liquid. The bromine derivatives of methane are of little importance, and may be prepared by methods analogous to those adopted for the preparation of the corresponding chlorine derivatives.

The iodine derivatives are of greater utility, and two of them, methyl iodide, CH_3I, and iodoform, CHI_3, are prepared on a considerable scale, the former for use in the laboratory, and the latter for use in medicine and surgery.

Methyl Iodide, CH_3I.

Methyl iodide may be prepared by the action of hydriodic acid on methyl alcohol, according to the equation—

$$CH_3OH + HI = CH_3I + HOH,$$

but it is more convenient to prepare it by a method analogous to that which is used in the preparation of hydriodic acid itself. Hydriodic acid is most readily obtained by the action of water on phosphorus iodide, the phosphorus iodide being formed by the interaction of iodine and red phosphorus. The equation for this reaction is—

$$PI_3 + 3HOH = H_3PO_3 + 3HI.$$

Now if, instead of water, we employ methyl alcohol, then the product of the reaction is methyl iodide, and not hydrogen iodide. The equation in this case is—

$$PI_3 + 3CH_3OH = H_3PO_3 + 3CH_3I.$$

The action is carried out by mixing methyl alcohol with red phosphorus and adding the requisite quantity of iodine in small portions at a time, in order to prevent the action from becoming too violent. The methyl iodide distils off from the warm mixture, is condensed, washed with water to remove alcohol, dried with calcium chloride, and distilled. It is a colourless liquid of high specific gravity, and boils at 45°. It is chiefly used for the purpose of introducing the methyl group

into organic compounds. When rubbed into the skin it speedily raises a blister.

Iodoform, CHI_3.

Just as chloroform is prepared from ethyl alcohol or acetone by the action of alkaline solution of a hypochlorite produced from bleaching powder and water, so the corresponding iodine compound, iodoform, is prepared from the same substances by the action of an alkaline solution of a hypo-iodite. The preparation is generally carried out by adding iodine in small quantities at a time to alcohol of about 20 per cent. strength which contains either caustic potash or potassium carbonate dissolved in it. Iodine acts upon the alkali with production of hypo-iodite, which at the temperature employed, about 70°, at once attacks the alcohol or acetone and converts it into iodoform. The action on alcohol may be represented by the equation—

$$\underset{\text{Ethyl alcohol}}{C_2H_5OH} + 8I + 6KOH = \underset{\text{Iodoform}}{CHI_3} + \underset{\text{Pot. formate}}{H.CO_2K} + 5KI + 5H_2O.$$

The iodoform separates out as a yellow precipitate, which is filtered off, and may be purified by recrystallisation from dilute alcohol. Iodoform is a solid, and melts at 120°. It is almost insoluble in water, sparingly soluble in alcohol at the ordinary temperature, but dissolves readily in ether, chloroform, etc. It may easily be recognised by its characteristic odour. On account of its antiseptic properties it is largely used in dressings for sores and wounds.

$$C_2H_5OH + 2HI = C_2H_6 + H_2O + I_2$$

CARBOHYDRATES.

STARCH, DEXTRIN, SUGAR.

It has been noted that formaldehyde under certain conditions polymerises with formation of sugars which have the formula $C_6H_{12}O_6$. Now, such sugars, and substances more or less closely related to them, form the bulk of the organic material in plants. The source from which plants derive the elements which give rise to the formation of these substances can only be the soil or the air. From the soil they receive moisture, and from the air carbon dioxide. If we assume for a moment, which is by no means improbable, that formaldehyde is the first substance produced by the plant's activity in the elaboration of the sugars, it is clear that the plant in producing formaldehyde from carbonic acid must get rid of superfluous oxygen, as appears in the following equation :—

$$H_2O + CO_2 = H_2CO + O_2.$$

As a matter of fact, plants, while they are absorbing carbon dioxide, are known to give off oxygen freely.

The reverse of this process takes place in the animal body. Sugars, and similar substances which serve as animal food, are oxidised by means of the oxygen inhaled from the air to carbon dioxide and water. Thus there is a continuous cycle of chemical action, plants giving out oxygen and absorbing carbon dioxide and water, whilst animals absorb oxygen and give out carbon dioxide and water.

Sugars found in plants have generally either the formula $C_6H_{12}O_6$, for example, grape-sugar and fruit-sugar; or else the formula $C_{12}H_{22}O_{11}$, for example, cane-sugar. Besides these substances, which are all freely soluble in water, plants contain other compounds of the same general character which are not soluble in water. Of these, the chief are **starch** and **cellulose**,

which have both the empirical formula $C_6H_{10}O_5$. It will be observed that in all of these compounds, $C_6H_{12}O_6$, $C_{12}H_{22}O_{11}$, and $C_6H_{10}O_5$, the hydrogen and oxygen are present in the proportions necessary to form water, the other constituent being carbon. Such compounds have thus the composition of a hydrate of carbon, and have therefore been termed **carbohydrates**. The term carbohydrate must not, however, be accepted in its original meaning in too strict a sense. Many compounds which have not the hydrogen and oxygen in the proportions necessary to form water are now termed carbohydrates, whilst there are many substances which have these elements in the requisite proportion and are yet not classified with the carbohydrates. The name, in fact, is used to include sugars, dextrins, starch, and cellulose. Any substance belonging to one of those groups is termed a carbohydrate, whether it corresponds in formula to the original definition or not, and substances such as formaldehyde, CH_2O, and acetic acid, $C_2H_4O_2$, are not termed carbohydrates, though they contain only carbon and the elements of water, because they belong to none of the above classes.

A brief outline of the chemistry of starch, dextrin, and simple sugars is given here, the detailed treatment of the sugars being reserved to a later stage.

Starch, $C_6H_{10}O_5$.

Starch has the empirical formula $C_6H_{10}O_5$, but we are without knowledge of its true molecular formula, as it is not volatile and does not yield true solutions in any solvent. It forms a reserve substance in plants, which have the power of converting sugars dissolved in their sap into starch, and depositing it in certain parts of the plant as a solid. When the circumstances of the plant require it, this solid starch can be reconverted into the soluble sugars and pass again into the sap of the plant.

As starch occurs already formed in plants, its commercial preparation from these plants is not, strictly speaking, a chemical process, but merely one of freeing it from other substances which occur along with it. In Europe, starch is manufactured chiefly from potatoes, wheat, and rice; in America it is manufactured

chiefly from wheat and maize. Starch occurs in plants in the form of small granules which, according to the plant, vary greatly in shape and size. They generally present an appearance as if they were made of successive concentric shells, like those of an onion.

The following is an outline of the process adopted for the preparation of potato starch. The potatoes, which contain about 75 per cent. of their weight of water and only about 20 per cent. of starch, are, first of all, carefully freed from grit, etc., by washing in a revolving drum with water, the potatoes being scraped clean by rubbing against each other and against brushes with which the drum is provided. After this process of cleansing, the potatoes are next cut up or rasped in a machine provided with numerous knife-edges or saw-teeth. It is necessary that this process should be very thorough, because the starch granules of the potato are contained in little sacs of cellulose which must be broken before the granules can escape and be further utilised. The pulp obtained by this rasping process is then passed through sieves along with water. These sieves have a mesh of such size that the bulk of the fibre and cellulose membrane is kept back, while the small starch granules pass through. The milky liquid is subjected to a further process of sifting through a finer mesh, and is then allowed to settle. The starch separates out as a layer from which the water can be afterwards withdrawn. It is then slowly dried at a moderate temperature, the cake produced cracking and breaking up into the familiar irregular, prismatic fragments.

Starch does not dissolve in cold water, but when heated with water to about 70° the wall of the starch granule swells and bursts, the contents escaping and passing into the water in the state of colloidal solution. If the colloidal solution is concentrated it sets to a jelly-like mass (starch paste) on cooling; when the solution is dilute it does not gelatinise. The best test for starch, whether in solution or in the solid state, is the blue colour produced by a solution of iodine in potassium iodide. This coloration is frequently used as a test for iodine, and it is equally useful as a test for starch. Starch solution made in this way may be filtered, a small quantity of gelatinous material remaining

behind on the filter whilst the bulk passes through as a clear solution.

Soluble starch may be prepared by soaking ordinary starch for several days in cold dilute hydrochloric acid. When the starch has been washed with cold water until free from hydrochloric acid, and is then dried at the ordinary temperature, it forms a white amorphous powder which readily dissolves in warm water, giving a clear solution. This solution is still of a colloidal nature, and the starch in it will not pass through an animal or vegetable membrane. Like ordinary starch solution, it gives a blue coloration with iodine. Soluble starch may be thrown out of aqueous solution by the addition of alcohol, in which it is insoluble. When soluble starch is dissolved in formamide, the freezing-point depression (p. 18) of the solutions so obtained indicates a molecular formula of $(C_6H_{10}O_5)_4$.

When starch is boiled with dilute acid, it is gradually converted, first into dextrin, and then into glucose. The formation of glucose may be represented by the equation—

$$\underset{\text{Starch}}{C_6H_{10}O_5} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6}.$$

Here the insoluble starch is converted into a soluble sugar. A similar transformation is brought about by the action of certain enzymes which exist both in plants and animals. By the term **enzyme** we understand an organic chemical substance which in many respects resembles in its action the catalytic substances of inorganic chemistry. There are certain important differences, however, which must be noted. In the first place, the activity of enzymes is destroyed by a very moderate rise in temperature, and there is for each one a particular temperature, generally about 40°, at which its activity is at a maximum. At the freezing-point they are generally inactive, and at the boiling-point they are gradually destroyed. Although they resemble ordinary catalysts in being active in very small concentrations, they differ from them inasmuch as they lose their activity when a certain amount of the substances on which they act has been transformed. This amount may be large, but it is not, as in the case of the inorganic catalysts, practically infinite. The enzyme is thus in the process of its activity gradually destroyed, unlike an inorganic catalyst, which persists

unchanged. It should be noted that enzymes are specific in their action; that is, a certain definite enzyme is required to bring about a particular transformation. The enzyme which effects the conversion of starch into sugar is called amylase or diastase. The termination *ase* is always employed in naming enzymes.

Diastase or **amylase** exists in saliva (the salivary diastase being also known as ptyalin), and likewise in the pancreatic juice. Starch, then, which is a large constituent of vegetable foods, is converted in the mouth and alimentary canal by this diastase into soluble sugars which may, after further change, be absorbed into the system. A solution of starch kept in the mouth for a few minutes ceases to give any coloration with iodine, having in this short time been completely converted into sugar.

Diastase also occurs in many germinating plants, and use is made of this in the process of **malting**, for the production from starch of the fermentable sugar used as a source of ethyl alcohol. This process will be referred to in the description of the manufacture of alcohol. The sugar produced by the action of diastase on starch is not glucose, $C_6H_{12}O_6$, but maltose, $C_{12}H_{22}O_{11}$.

Dextrin, $C_6H_{10}O_5$.

It has been stated above that dextrin is an intermediate substance in the production of sugar from starch. More than one substance is known under the name of dextrin, and ordinary samples consist of a mixture of various compounds. They may all be represented by the formula $C_6H_{10}O_5$, but we are without proper knowledge of their true molecular weight. The molecule is less complex than that of starch, but more complex than that of a soluble sugar. The dextrins dissolve in water to form gummy solutions which are partly, no doubt, true solutions and partly colloidal.

Dextrin exists in certain vegetable juices, and may most readily be produced on the commercial scale by the action of heat on starch. The conversion of starch into dextrin takes place at a temperature of about 200°, and on a large scale the heating may be carried out by means of superheated steam. To prevent charring, the temperature is not allowed to exceed

250°. One of the chief chemical changes that occur in toasting bread is the conversion of a portion of the wheat starch of the flour into dextrin. The crumb of wheaten bread is practically insoluble in water, but it will be found that an aqueous extract from a piece of toast contains a considerable amount of dissolved material. Again, when starched linen is ironed, the heat of the iron converts the starch with which it comes into contact into a glossy layer of dextrin.

Dextrin may either give no coloration with iodine in potassium iodide, or it may give a red coloration, according to the variety dealt with. The commercial product invariably contains small quantities of starch and of glucose. It is used principally for the manufacture of adhesives.

Commercial Glucose, $C_6H_{12}O_6$.

The term glucose is used in two different senses: it is applied, from the strictly chemical point of view, to a pure sugar also known as dextrose, the special properties of which will be dealt with later. It is also applied to a commercial product produced by boiling starch with dilute mineral acids. This commercial glucose may contain 90 per cent. of dextrose, but it also invariably contains dextrin, which, as we have seen, is an intermediate product in the conversion of starch into a sugar. The conversion of starch into glucose is generally effected in closed vessels into which steam at three or four atmospheres pressure is admitted. The acid used, which may be either hydrochloric acid or sulphuric acid, is dilute, and generally contains not more than 3 per cent. of acid. Under these conditions the conversion is practically completed in about an hour. The excess of acid is removed by means of sodium carbonate or chalk, and the liquid is decolorised by running through filters containing bone charcoal. It is then concentrated by evaporation, refiltered through fresh charcoal, and evaporated in a vacuum pan until it reaches the crystallising point, or, if so desired, remains as a concentrated syrup. Large quantities of glucose are used in the preparation of syrups, preserved fruits, and confectionery, in dressings for the preparation of textiles, etc. The sugars which it contains are also used in the production of alcohol by fermentation.

Glucose when warmed with Fehling's solution (a deep-blue solution containing copper sulphate, alkaline tartrate, and excess of caustic soda) decolorises it and produces a red precipitate of cuprous oxide, formed from the cupric compound by reduction.

ALCOHOLIC FERMENTATION.

When yeast is allowed to grow in a solution containing sugar it secretes various enzymes, amongst which one named **zymase** has the power of converting dextrose into ethyl alcohol and carbon dioxide, according to the equation—

$$C_6H_{12}O_6 = 2C_2H_5.OH + 2CO_2.$$

Such a process is generally known as a fermentation, and the living substance (in this case the yeast plant) which caused the fermentation was termed the ferment. It was at first thought that the process of fermentation depended on the vital process in the living organism, but it has been shown that an extract of yeast cells containing no living matter whatever is capable of inducing fermentation. We, therefore, now attribute the alcoholic fermentation of sugar, not to the yeast plant directly, but to the enzyme zymase which it contains.

According to the nature of the liquid to be fermented and to the conditions of the fermentation, the character of the alcoholic product varies. Thus, wine is produced by the fermentation of the sugar contained in ripe grapes; beer, by the fermentation of sugars derived from the starch of barley; rectified spirit, by the fermentation of sugars derived from potato starch or other similar commercial starches.

Brewing.

The process of brewing affords an interesting illustration of the action of various enzymes. The raw material is the grain of barley. The raw grain contains practically no sugar, but an abundant supply of starch, and the first process necessary

to secure alcoholic fermentation is the conversion of this starch into sugars on which the yeast can act. In order to effect this conversion the barley is **malted**, a process which essentially consists in the sprouting and drying of the grain. The grain is first steeped for some days in water. During this process it swells and softens, and it is then piled on the malting floor, where it is kept well aired, and moistened from time to time as required. After some time the grain begins to heat, the heating indicating the commencement of the process of sprouting or germination. It is then spread in a shallower layer on the malting floor, and the germination proceeds until after five or six days it has reached the proper point. In order now to stop the growth of the young plant, the grain is dried at a temperature at first of about 50° and afterwards at about 100°. The dried grain is then brushed clean, and constitutes the malt of commerce. During the process of germination two enzymes have developed in the malt: one **diastase** or **amylase**, which is capable of converting starch into sugar; and another, **peptase**, which is capable of destroying albuminous matter.

The malt is now mixed with water in mash tuns, and heated to a temperature of about 60°. The two enzymes act rapidly at this temperature on the starch and albuminous material which the malt contains, converting them into soluble products: the starch into dextrins and maltose, the albuminous substances into soluble peptones and amino acids. It is customary to add extra starch to the mash in the form chiefly of raw grain, *i.e.* unmalted barley, in order to utilise fully the diastatic power of the malt. The starch in this unmalted grain undergoes the same changes as the starch in the malt itself.

The filtered wort from the mash tuns is then boiled for some time in order thoroughly to sterilise it, to precipitate the albuminous matter which still remains, and also to concentrate the liquor. During this process of boiling, hops are added to impart a bitter flavour to the beer, and also to protect to some extent the finished product from acid fermentation.

The next process is the fermentation of the wort by means of yeast. Yeast consists of a mixture of plant cells belonging to various species of *Saccharomyces*. For brewing purposes yeasts of certain definite strains are employed, and the so-

called wild yeasts are carefully excluded. According to the temperature employed, the beer may be made by either top fermentation or bottom fermentation. In the former case, where the temperature is about 16°, the fermentation is so rapid that the carbon dioxide evolved carries the yeast cells to the surface, where they remain; in the latter case, where the temperature is about 6°, the fermentation is so slow that the yeast cells are not buoyed up by the gas, but remain in the bottom of the brewing vessel. Top fermentation is mostly used in this country; bottom fermentation for the production of the Continental lager beer.

Besides zymase, to which the alcoholic fermentation proper is due, yeast contains the enzyme **invertase**, which can effect the conversion of cane-sugar or sucrose into the two simpler sugars, glucose and fructose, according to the equation—

$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Fructose}}{C_6H_{12}O_6};$$

and also **maltase**, which can similarly resolve maltose into the directly fermentable sugar glucose—

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose}}{2C_6H_{12}O_6}.$$

The first action of the yeast, therefore, is to convert the maltose into glucose, and then, by means of the enzyme **zymase**, to ferment the glucose so produced. Although the production of ethyl alcohol and carbon dioxide from glucose is the chief reaction in the fermentation, other substances are produced at the same time; for example, glycerol and succinic acid. The fermentation ceases before the whole of the sugar is converted into alcohol, and the liquor after filtration is then ready for storage.

In the fermentation of grape-juice for **wine** no yeast is added, as the ferment, a species of *Saccharomyces*, exists on the grape itself.

Distilled spirits are prepared, as the name implies, by careful distillation of the crude fermented liquor. According to the source of the sugar which is fermented, different products are obtained. Thus, rum is prepared by distilling the products

of fermentation of cane-sugar molasses; brandy is prepared by distilling wine; and whisky, by distillation of a liquor prepared by the fermentation of malt.

Industrial Alcohol.

For industrial and scientific purposes alcohol is prepared by the fermentation of sugars derived either from starch by the action of acid or diastase, or from the molasses of cane- or beet-sugar. Here the starch is converted as completely as possible into fermentable sugar, and the fermentation is allowed to proceed to an end. A crude product is obtained containing up to 13 per cent. of ethyl alcohol, which is then separated from water and impurities by distillation in specially constructed stills. The raw spirit still contains aldehydes, and a mixture of other higher-boiling alcohols known as **fusel oil**. The aldehydes may be removed by treatment first with caustic soda and then with dilute sulphuric acid, and the fusel oil may, for the most part, be got rid of by filtration through bone charcoal. The purified alcohol is carefully redistilled in a rectifying still or dephlegmator, the chief product from which is rectified spirit. The rectified spirit of the Pharmacopœia should contain 90 per cent. of alcohol by volume. If pure or absolute alcohol is desired, the rectified spirit is left for some time in contact with quicklime, which absorbs the water and has no action on the alcohol, which is then distilled off from the lime. Alcohol may be got in this way of over 99 per cent. strength.

Besides these pure or aqueous alcohols there are in extensive use alcohols which have been deliberately rendered impure in order to make them unpalatable. These are known in Britain as **methylated spirit**, of which two varieties exist, and may be used without payment of Excise duty. Industrial methylated spirit, which can only be used under certain restrictions, is made by the addition to rectified spirit of 5 per cent. of wood naphtha. Mineralised methylated spirit contains, in addition to 10 per cent. of wood naphtha, about 0·4 per cent. of petroleum oil (mineral naphtha). In the United States 0·5 per cent. of benzene is added instead of mineral naphtha. Alcohol is chiefly used in industry as a combustible and as a solvent.

Ethyl Alcohol, C_2H_5OH.

Ethyl alcohol is a colourless liquid which has a specific gravity of 0·794 at the ordinary temperature, and a boiling-point of 78°. It burns with a non-luminous or very feebly luminous flame according to the conditions, and its vapour may form explosive mixtures with air. It mixes with water in all proportions, the mixing of the liquids being accompanied by slight evolution of heat and considerable contraction of volume. Thus, if we mix 50 c.c. of alcohol and 50 c.c. of water, the resulting mixture does not occupy 100 c.c., but only 97·5 c.c. The concentration of an alcohol solution is generally ascertained by determining its specific gravity, the relation between specific gravity and quantity of alcohol in the solution being given in accurate tables which have been drawn up for the purpose. The composition of such solutions is either expressed in parts by weight of alcohol per cent., or in parts by volume per cent. For example, an alcohol of specific gravity 0·872 is given in the tables as containing 70 per cent. of alcohol by weight or 77 per cent. of alcohol by volume. What is known as **proof spirit** contains 49 per cent. of alcohol by weight or 57 per cent. by volume, and has a specific gravity of 0·920. Spirits which have more alcohol than this are said to be overproof, and those which have less, underproof.

The chief physiological action of alcohol is narcotic. It is largely used in the Pharmacopœia on account of its solvent properties for the preparation of the so-called **tinctures**, which are alcoholic solutions of various substances that do not readily dissolve in water. Slightly diluted rectified spirit is used for the purpose of sterilising the skin of patients and the hands of operators.

The chemical properties of ethyl alcohol are similar to those of methyl alcohol. It reacts with sodium to form sodium ethoxide and hydrogen according to the equation—

$$2CH_3.CH_2.OH + 2Na = 2CH_3.CH_2.ONa + H_2.$$

Since it contains the group $CH_2.OH$ it is a primary alcohol, and therefore yields on oxidation an aldehyde, $CH_3.CHO$, acetaldehyde, and an acid, $CH_3.COOH$, acetic acid.

HYDROCARBONS CONTAINING TWO ATOMS OF CARBON.

ETHANE, ETHYLENE, AND ACETYLENE.

Ethane, C_2H_6, is the saturated hydrocarbon corresponding to ethyl alcohol, from which it may be obtained in small quantity by heating to a high temperature with concentrated hydriodic acid solution—

$$C_2H_5OH + 2HI = C_2H_6 + H_2O + I_2.$$ c.f. p 570

It occurs in natural gas, but not to the same extent as methane, and may be conveniently prepared in the laboratory by the electrolysis of a concentrated solution of potassium or sodium acetate. When either of these salts is electrolysed, hydrogen comes off at the cathode, and a mixture of carbon dioxide and ethane at the anode. These gases result from the action of two discharged acetate radicals on each other, the equation representing the reaction being as follows :—

$$2CH_3.COO = \underset{\text{Ethane}}{CH_3.CH_3} + 2CO_2.$$

The carbon dioxide may be readily absorbed by means of a solution of caustic potash, which leaves ethane unaffected.

Ethane may also be prepared by passing a mixture of ethylene and hydrogen over finely divided nickel at the temperature of 200°—

$$C_2H_4 + H_2 = C_2H_6.$$

Ethane resembles methane very closely in its properties, but differs from it in being condensable to a liquid at the ordinary temperature. Like methane, it is attacked with difficulty by ordinary chemical reagents.

Ethylene, C_2H_4, may be prepared from alcohol by direct decomposition according to the following equation—

$$\underset{\text{Ethyl alcohol}}{C_2H_6O} = \underset{\text{Ethylene}}{C_2H_4} + H_2O.$$

This action can be carried out in practice by passing the vapour of alcohol over aluminium hydroxide heated to a temperature of 360°. Ethylene is prepared on a large scale

in this way, but in the laboratory it is usually prepared by the action of concentrated sulphuric acid, or of syrupy phosphoric acid on ethyl alcohol. The action of these acids is not, as might be supposed, a purely dehydrating action. For example, in the case of sulphuric acid the intermediate compound, ethyl hydrogen sulphate, is first formed according to the equation,

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O,$$

and then is decomposed by heat as follows :—

$$C_2H_5HSO_4 = C_2H_4 + H_2SO_4.$$

When concentrated sulphuric acid is used in the preparation it must be present in considerable excess, and the temperature must be kept at about 165°. At this temperature some of the sulphuric acid is reduced by the organic material with production of sulphur dioxide, which passes over with the ethylene and is removed by bubbling the gas through a solution of caustic alkali.

Ethylene is a colourless gas, but differs from methane and ethane by possessing a faint, sweetish odour. It dissolves more readily in water than these gases, and is easily reduced to the liquid state by pressure. It burns with a luminous flame, and it is to the presence of about 4 per cent. of ethylene that coal gas owes much of its luminosity.

Ethylene is what is termed an **unsaturated hydrocarbon,** and belongs to that class of unsaturated hydrocarbons which we term **olefines,** the name being derived from a former name of ethylene, viz., olefiant gas. This name, meaning the oil-forming gas, was given to ethylene on account of the power which it displays of combining directly with chlorine by addition, with production of an oily liquid. The equation representing this direct addition of ethylene and chlorine is as follows :—

$$C_2H_4 + Cl_2 = \underset{\text{Ethylene dichloride}}{C_2H_4Cl_2}.$$

It will be noticed that this action of chlorine on ethylene differs radically from the action of chlorine on methane, or indeed of any saturated hydrocarbon. In the case of the saturated hydrocarbons chlorine always reacts by substitution

of chlorine for hydrogen, with simultaneous production of hydrochloric acid. In the case of unsaturated hydrocarbons no hydrochloric acid is produced, the two molecules directly uniting to form a single molecule.

In the same way ethylene unites with bromine to form ethylene dibromide, a pleasant smelling oil of similar properties to ethylene dichloride. These two actions may be taken as actions typical of the unsaturated hydrocarbons, and indeed, may be applied to distinguish between saturated and unsaturated hydrocarbons. If bromine is dissolved in dry chloroform and brought into contact with an unsaturated hydrocarbon, the colour of the bromine speedily disappears. On the other hand, a saturated hydrocarbon has practically no effect on the colour.

Another test, **Baeyer's test**, is often used to distinguish unsaturated from saturated substances. If a solution of an unsaturated substance is made slightly alkaline with sodium carbonate, and if a few drops of dilute solution of potassium permanganate are added in the cold, the colour of the potassium permanganate is at once discharged. Saturated substances under these conditions have no effect on the permanganate.

The graphic formula of ethylene is generally written as follows:—

$$\begin{array}{c} H-C=C-H \\ \;\;|\;\;\;\;\;| \\ \;\;H\;\;\;H \end{array} \quad \text{or} \quad H_2C : CH_2.$$

The "double bond" between the carbon atoms must not be interpreted literally as indicating firmer union than a single bond. The reverse is the case, for it is a general rule that a chain of carbon atoms may be split more readily, say by oxidising agents, at a double bond than at a single bond.

Acetylene, C_2H_2, is prepared by the action of water on calcium carbide—

$$CaC_2 + 2H_2O = Ca(OH)_2 + C_2H_2.$$

The action takes place briskly at the ordinary temperature, with evolution of a considerable amount of heat. When prepared in this way from commercial carbide, acetylene has an unpleasant smell due to the presence of impurities such as phosphine, PH_3, derived from traces of calcium

phosphide in the carbide. When pure, its smell resembles that of ethylene.

Acetylene occurs in small quantity (about 0·06 vol. per cent.) in coal-gas, and ten times this amount may be found in the gases issuing from a Bunsen burner which has struck back. In the latter case the coal gas has been burnt in a very defective supply of air, with consequent production of acetylene.

Pure acetylene resembles ethylene closely in its physical properties. It may be condensed by pressure to the liquid state, and at the ordinary temperature it dissolves in about its own volume of water. It is not markedly poisonous when pure, but commercial acetylene may be dangerously poisonous owing to the phosphine and other impurities which it contains.

Acetylene burns with a brightly luminous flame and is used extensively as an illuminant. When burned in a restricted supply of air, it gives rise to a very smoky flame, from which the carbon that has escaped combustion may be collected and prepared for use as lamp-black. When mixed with oxygen in the proportions given by the following equation—

$$\underset{\text{2 vols.}}{2C_2H_2} + \underset{\text{5 vols.}}{5O_2} = 4CO_2 + 2H_2O,$$

it forms a very explosive mixture, and violent explosions may even occur with comparatively small volumes of mixtures of acetylene and air. When burned with oxygen in a blowpipe it produces a flame of very high temperature, which is used for cutting steel plates, etc. Acetylene is what is termed an *endothermic* compound, *i.e.*, one formed from its elements with absorption of heat. Consequently, when decomposed into its elements again it evolves a like amount of heat, with consequent great elevation of temperature and increase of activity. When subjected to shock or to the passage of an electric spark, acetylene even in absence of air or oxygen may decompose explosively into its elements. This property renders inadvisable the storage of the gas in large quantities, or the use of acetylene in the liquid state.

Acetylene, like ethylene, is an unsaturated compound, readily reducing alkaline permanganate in the cold, and

combining with chlorine or bromine according to the following equations :—

$$C_2H_2 \quad + \quad 2Cl_2 \quad = \quad \underset{\text{Acetylene tetrachloride}}{C_2H_2Cl_4}$$

$$C_2H_2 \quad + \quad 2Br_2 \quad = \quad \underset{\text{Acetylene tetrabromide}}{C_2H_2Br_4}$$

Acetylene may easily be distinguished from ethylene, however, by the peculiarity that its hydrogen atoms are replaceable by metals. Thus when acetylene is led over heated sodium the following reaction occurs :—

$$C_2H_2 + 2Na = C_2Na_2 + H_2.$$

Calcium carbide, C_2Ca, is the corresponding calcium compound. When acetylene is led into an ammoniacal solution of cuprous chloride a red precipitate, usually called copper acetylide, is produced, which, when dried, is highly explosive and has the composition C_2Cu_2. The production of this red compound is utilised for the detection of small quantities of acetylene.

The constitutional formula of acetylene is usually written $H—C{\equiv}C—H$, or $HC \vdots CH$, with a triple bond between the carbons. Wherever the grouping $C{\equiv}C—H$ occurs, the hydrogen atom is replaceable by metals.

COMPOUNDS DERIVED FROM ETHYL ALCOHOL.

ETHYL CHLORIDE, BROMIDE, IODIDE, AND OXIDE.

Just as methyl chloride, bromide, and iodide may be derived from methyl alcohol, so ethyl chloride, C_2H_5Cl, ethyl bromide, C_2H_5Br, and ethyl iodide, C_2H_5I, may be derived from ethyl alcohol, the hydroxyl group of the alcohol being replaced by the halogen.

Ethyl chloride, C_2H_5Cl, is prepared by the action of gaseous hydrochloric acid on ethyl alcohol, and is also obtained as a secondary product in the manufacture of chloral. It may be produced readily by the action of ethyl alcohol of the chlorides of phosphorus, according to the equations :—

$$3C_2H_5OH + PCl_3 = 3C_2H_5Cl + H_3PO_3$$
$$C_2H_5OH + PCl_5 = C_2H_5Cl + POCl_3 + HCl.$$

These reactions are precisely analogous to the action of the chlorides of phosphorus on water—

$$3HOH + PCl_3 = 3HCl + H_3PO_3$$
$$HOH + PCl_5 = HCl + POCl_3 + HCl,$$

and in general it may be said that most organic compounds containing a hydroxyl group attached to a carbon atom are capable of having this hydroxyl group replaced by chlorine by the action of phosphorus trichloride or phosphorus pentachloride.

Ethyl chloride is a liquid which boils at 12°, so that at ordinary room temperatures it is gaseous. It is used both as a general anæsthetic by inhalation, and as a local anæsthetic by the cold produced on evaporation of the liquid. It is generally supplied either in sealed glass tubes or in metal cylinders.

Ethyl bromide, C_2H_5Br.—Ethyl bromide is prepared from ethyl alcohol by the action of phosphorus and bromine, that is, of phosphorus tribromide—

$$3C_2H_5OH + PBr_3 = 3C_2H_5Br + H_3PO_3.$$

Like the chloride, it may be used either as a general or a local anæsthetic. It is a colourless liquid about half as heavy again as water, and boils at 39°.

Ethyl iodide, C_2H_5I.—Ethyl iodide is prepared by slowly adding iodine to a warm mixture of ethyl alcohol and red phosphorus. The phosphorus and iodine combine, and the resulting iodide of phosphorus acts upon the alcohol with production of ethyl iodide—

$$3C_2H_5OH + PI_3 = 3C_2H_5I + H_3PO_3.$$

Ethyl iodide is a liquid which is colourless when pure, but which gradually acquires a yellow or reddish colour on exposure to air and light, owing to the production of small quantities of iodine. It is about twice as heavy as water, and boils at 72°. It has an anæsthetic action when the vapour is inhaled, but is not used for the production of complete anæsthesia.

Ethyl Oxide or Ethyl Ether, $(C_2H_5)_2O$.

It has been stated that sodium ethoxide, $NaOC_2H_5$, may be formed by the action of sodium on ethyl alcohol. This compound when brought into contact with ethyl bromide or iodide reacts with these substances, with production of sodium bromide or iodide and of ethyl ether, $C_2H_5 . O . C_2H_5$—

$$C_2H_5Br + NaOC_2H_5 = NaBr + C_2H_5.O.C_2H_5.$$

Ethyl ether is thus the oxide of the radical ethyl, as ethyl alcohol is the hydroxide of the radical ethyl. It may, therefore, be looked upon as in a sense an anhydride of ethyl alcohol, and may actually be derived from ethyl alcohol by removal of the elements of water—

$$2C_2H_5OH = (C_2H_5)_2O + H_2O.$$

It is manufactured by a process which would suggest that alcohol is directly dehydrated, namely, by the action on it of concentrated sulphuric acid. The dehydration, however, is not a direct one, but takes place in two stages which may be easily followed. Ethyl alcohol is mixed with about twice its weight of concentrated sulphuric acid and heated to a temperature of about 140°. At this temperature ether begins to distil over, and alcohol is run slowly in from a tap-funnel to replace that which has been converted into ether. That the process is not one of direct dehydration by the sulphuric acid is evident from the fact that water passes over along with ether and is not retained by the acid. The first action which takes place is the formation of ethyl hydrogen sulphate, according to the equation (*cf.* p. 64)—

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + HOH.$$

In this substance one hydrogen atom of sulphuric acid is replaced by the radical ethyl, but the other hydrogen is still replaceable by a metal, and therefore the substance has acid properties and often called **sulphovinic acid**. This substance when heated with alcohol reacts with it according to the equation—

$$C_2H_5OH + C_2H_5.HSO_4 = C_2H_5.O.C_2H_5 + H_2SO_4,$$

ether and sulphuric acid being formed. The sulphuric acid

thus produced can now react with more alcohol, so that a comparatively small quantity of it is capable of converting a large amount of alcohol into ethyl ether.

The ether which is condensed contains small quantities of alcohol, water, and sulphur dioxide, produced by reduction of sulphuric acid. It is freed from these impurities by washing it in a separating funnel with a dilute solution of alkali, after which it is dried with calcium chloride and distilled. A separating funnel is shown in Fig. 13. The upper layer represents the ether, and the lower layer the water or aqueous solution, in which the ether is only slightly soluble. The aqueous liquid may be withdrawn through the tap, and the ether shaken up with a fresh portion added through the neck, which is tightly stoppered during shaking.

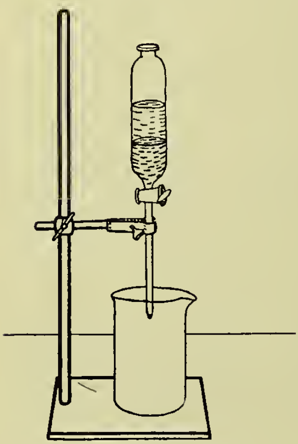


FIG. 13.

Ethyl ether is a colourless mobile liquid of sp. gr. 0·72, which boils at 35°. The vapour which it produces is very inflammable, so that care must be used in handling it in the neighbourhood of a flame, especially when the atmospheric temperature is high, for then it gives off vapour freely, owing to its low boiling-point.

Ether differs from alcohol in being comparatively inactive from the chemical point of view. It is chiefly used as a solvent for organic substances, and for the production of both general anæsthesia by inhalation, and of local anæsthesia by cooling the part to which a spray of the liquid is applied.

ALDEHYDES.

Acetaldehyde, C_2H_4O.

Acetaldehyde is a much more typical representative of the class of aldehydes than formaldehyde. It is prepared by the oxidation of ethyl alcohol by means of chromic acid mixture. This mixture, which is very often used as an oxidising mixture

in organic chemistry, is made by the addition of sulphuric acid to potassium dichromate and water. When ethyl alcohol is added to such a mixture oxidation at once begins, and is accelerated when the mixture is heated. The experiment is often carried out in a test-tube for the detection of ethyl alcohol, the production of acetaldehyde being at once evident when the tube is heated, from the characteristic smell of the compound. The reddish solution of potassium dichromate becomes, at the same time, darker and ultimately green by the production of chromic sulphate. When the reaction is used for

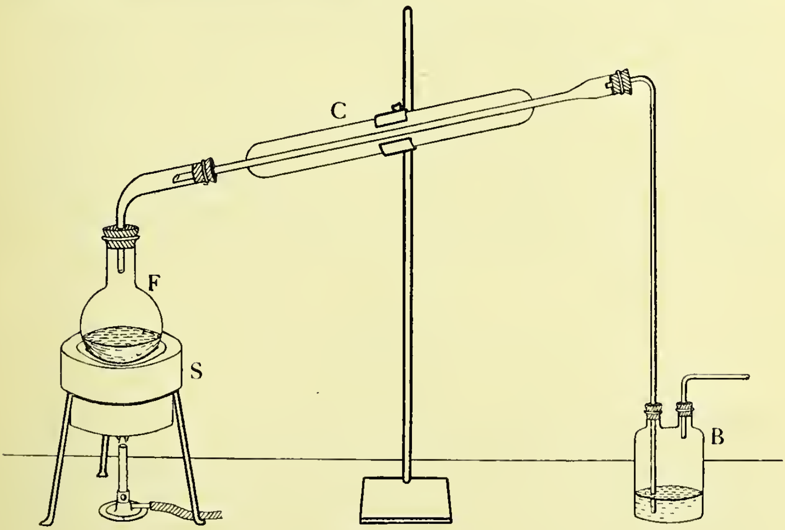
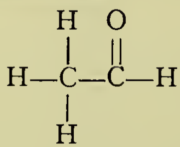


FIG. 14.

the preparation of aldehyde (Fig. 14), the mixture is heated on a steam-bath (S), in a flask (F) connected with a reflux condenser (C), through which slightly warm water circulates. The object of this condenser is to allow the acetaldehyde, which boils at about 20°, to pass on as vapour, while any ethyl alcohol which may boil off is condensed and returned to the reaction flask for oxidation. The vapours from the condenser are generally led into a vessel (B) containing ether, in which they dissolve, the ether being kept cool by immersion in cold water or crushed ice. When sufficient aldehyde has been collected in ether, the ethereal solution is saturated in the cold with ammonia

gas. Combination between the acetaldehyde and ammonia takes place, a solid compound called aldehyde-ammonia, C_2H_4O,NH_3, being formed, which crystallises from the ethereal solution and may be filtered off. In this way acetaldehyde is separated from the small quantities of ethyl alcohol and other products which pass along with it into the ether. To obtain acetaldehyde from aldehyde-ammonia, it is only necessary to warm the latter with dilute sulphuric acid, which combines with the ammonia and liberates the aldehyde as vapour, which can afterwards be condensed, dried, and purified by redistillation.

Acetaldehyde is a colourless liquid of about the same specific gravity as alcohol, and, like other aldehydes, it boils at a much lower temperature than the alcohol from which it is derived by oxidation. On account of its low boiling-point, namely 21°, it is generally kept in sealed glass tubes or bottles. Acetaldehyde mixes with water, alcohol, and ether in all proportions, and is easily recognised by its characteristic odour, which is not unpleasant, and altogether different from the pungent odour of formaldehyde. Its graphic formula is—



which may be conveniently abbreviated to $CH_3.CO.H$ or $CH_3.CH:O$.

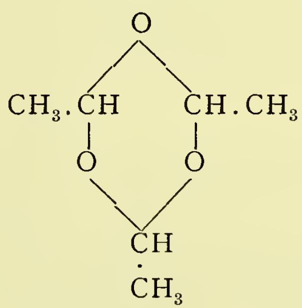
Like formaldehyde, acetaldehyde exhibits a great tendency to polymerise under the influence of dilute acids. Two substances are produced by its polymerisation, namely, metaldehyde and paraldehyde. **Metaldehyde** is a solid, and is produced when the polymerisation takes place at low temperatures. At the ordinary temperature the product is **paraldehyde**, which is a colourless liquid with a characteristic odour and a relatively high boiling-point, namely 124°. Both metaldehyde and paraldehyde have the formula $(CH_3.CO.H)_3$. Paraldehyde has about the same specific gravity as water, and is only soluble in water to the extent of 10 per cent. It is used in medicine as a sedative.

Aldehyde when exposed to air gradually acquires an acid

reaction, due to the production of acetic acid by union with atmospheric oxygen according to the equation—

$$2CH_3.CO.H + O_2 = 2CH_3.COOH.$$

Like formaldehyde, acetaldehyde has marked reducing properties, precipitating, for example, metallic silver from alkaline silver solutions. It should be noted that neither metaldehyde nor paraldehyde exhibit such reducing actions, and have no tendency to oxidise in air. This would point to these substances being not true aldehydes, that is, to their not containing the typical group of the aldehydes, CO.H, to which the reducing action is due. The formula generally attributed to them is—



Acetaldehyde exhibits the power shown by most other aldehydes of forming **addition compounds** with a considerable variety of substances. We have seen that it unites with the **ammonia** to form aldehyde-ammonia. The action may be represented by the equation—

$$CH_3.\overset{O}{C}.H + NH_3 = CH_3.\overset{\displaystyle OH}{\underset{\displaystyle NH_2}{C}}.H$$

and the mode of union in this case may be taken as typical. The hydrogen of the added molecule unites with the oxygen of the aldehyde group to form hydroxyl, and the rest of the added molecule unites with the carbon of the aldehyde group. Some aldehydes, for example, formaldehyde and benzaldehyde, $C_6H_5.CO.H$, do not unite directly with ammonia, but react with it with elimination of water.

Acetaldehyde unites freely with **sodium hydrogen sulphite**, $NaHSO_3$, to form the compound—

$$CH_3.\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle SO_3Na}{|}}{C}}.H$$

This compound though soluble in water is insoluble in a concentrated solution of the sodium bisulphite, so that when it is formed in such a solution it separates in the crystalline state. These bisulphite addition compounds are very often utilised in the process of separating and purifying aldehydes.

Under the influence of acids, acetaldehyde reacts with alcohol according to the following equation—

$$CH_3.CO.H + 2C_2H_5.OH = \underset{\text{Acetal}}{CH_3.\overset{OC_2H_5\ \ OC_2H_5}{\overset{\diagdown\ \diagup}{C}}.H} + H_2O.$$

The substance so produced is called **acetal**, and is formed in small quantity during the preparation of aldehyde, for there the aldehyde is produced in presence of ethyl alcohol and an acid.

Acetaldehyde reacts readily with hydroxylamine according to the equation,

$$CH_3.CH:O + H_2NOH = \underset{\text{Acetaldoxime}}{CH_3.CH:N.OH} + H_2O,$$

to form the substance known as **acetaldoxime.** The oximes, of which acetaldoxime is an example, are generally crystalline compounds, and are utilised in the detection and investigation of aldehydes.

A still more important reagent for aldehydes is the substance known as phenyl-hydrazine, $C_6H_5.NH.NH_2$. This substance reacts readily with aldehydes to form crystalline compounds, for the most part sparingly soluble in water, which are termed **phenyl-hydrazones.** Thus the phenyl-hydrazone of acetaldehyde is formed according to the equation—

$$CH_3.CH:O + H_2N.NHC_6H_5 = CH_3.CH:N.NH.C_6H_5 + H_2O.$$

Both the oximes and the phenyl-hydrazones may be hydrolysed by warming with dilute hydrochloric acid, the elements of water being taken up and the aldehydes being liberated according to equations which are the reverse of those just given.

Under the influence of a solution of an alkaline carbonate, one molecule of acetaldehyde reacts with another in the manner previously indicated for the formation of an additive compound. One molecule of aldehyde takes up one hydrogen atom from the methyl group of the second molecule so as to form the hydroxyl group, the rest of the molecule combining with the carbon of the original aldehyde group—

$$\underset{\text{Acetaldehyde}}{CH_3.\overset{O}{C}.H} + \underset{\text{Acetaldehyde}}{H.CH_2.CO.H} = \underset{\text{Aldol}}{CH_3.\overset{\overset{OH}{|}}{\underset{\underset{CH_2.CO.H.}{|}}{C}}.H}$$

The substance $CH_3.CH(OH).CH_2.CO.H$ produced in this way is termed **aldol**, and the process is known as the aldol condensation. This substance, which is in a sense a polymer of acetaldehyde, differs from paraldehyde and metaldehyde in still containing the aldehyde group $CO.H$, and in giving the reducing actions proper to aldehydes.

Chloral, $CCl_3.CO.H$.

Chloral, or trichloracetaldehyde, may be prepared by the action of chlorine on aldehyde. The chlorine in this case acts as it does on a hydrocarbon, the three hydrogens of the methyl group being replaced by chlorine according to the equation—

$$CH_3.CO.H + 3Cl_2 = CCl_3.CO.H + 3HCl.$$

Chloral, however, is generally prepared, not from acetaldehyde but from ethyl alcohol. Chlorine, it must be remembered, has not only the power of replacing hydrogen in a molecule, but also of acting as an oxidising agent by abstracting hydrogen from the molecule. Now, we may conceive that it acts upon ethyl alcohol in both of these ways, abstracting two atoms of hydrogen to form acetaldehyde and, at the same time, replacing hydrogen so as to form a trichloro-derivative. The total action

of chlorine on ethyl alcohol may therefore be represented as follows :—

$$CH_3.CH_2.OH + 4Cl_2 = CCl_3.CO.H + 5HCl.$$

The operation is carried out by saturating alcohol with chlorine, first in the cold, and afterwards at about 60°. When the action is over, a crystalline substance separates on cooling. This substance is not chloral itself, but an additive compound of chloral with ethyl alcohol, which is generally known as chloral alcoholate. The addition takes place in the ordinary way; the hydrogen of the hydroxyl group of the alcohol becomes added to the oxygen of the carbonyl group, CO, while the rest of the molecule is added to the carbon of the same group. We may thus write the formula of chloral alcoholate as follows :—

$$\begin{array}{c} HO \quad OC_2H_5 \\ \diagdown\!\diagup \\ CCl_3.C.H. \end{array}$$

From this substance chloral itself may be prepared by distillation with sulphuric acid.

The crude chloral thus obtained is purified by bringing it into contact with a small amount of water, with which it unites, forming the crystalline chloral hydrate corresponding to the chloral alcoholate. This substance is recrystallised and distilled with concentrated sulphuric acid, when chloral itself passes over.

Chloral is an oily liquid which is about half as heavy again as water, and boils at 97°. In its chemical action it behaves as a true aldehyde, and like other aldehydes tends readily to polymerise. On keeping, it passes slowly into an amorphous white substance known as metachloral. The same polymerisation takes place readily under the influence of acid. **Chloral hydrate**, on the other hand, does not exhibit this tendency to polymerise, and so it is in this form that chloral is invariably employed in medicine. When liquid chloral is brought into contact with water in the amount represented by the following equation—

$$CCl_3.CO.H + H_2O = CCl_3.CO.H,H_2O,$$

the two substances unite readily with evolution of heat, forming

the crystalline hydrate which melts at 57°. This so-called hydrate is really an aldehydrol, and its constitution may be represented by the formula $CCl_3.CH(OH)_2$. It has a characteristic odour resembling that of melons, is freely soluble in water, and is extensively used in medicine as a hypnotic.

When oxidised, chloral is converted into trichlor-acetic acid, thus—

$$CCl_3.CO.H + (O) = CCl_3.COOH.$$

One of the most interesting reactions in which chloral or chloral hydrate takes part is that exhibited with alkalies. When to a solution of chloral or chloral hydrate in water a few drops of caustic alkali are added, the solution immediately becomes turbid. The turbidity is caused by the separation of chloroform from the solution, and the action may be represented by the equation—

$$\underset{\text{Chloral}}{CCl_3.CO.H} + NaOH = \underset{\text{Chloroform}}{CHCl_3} + \underset{\text{Sodium formate}}{H.COONa.}$$

The action of bleaching powder on alcohol with production of chloroform may now be understood. We may look upon bleaching powder as a store of chlorine which acts upon the ethyl alcohol in the manner above described, with production of chloral, which is then further attacked by the calcium hydroxide which the bleaching powder always contains, and converted into chloroform and calcium formate.

Butylchloral, $C_3H_4Cl_3.CO.H$.

When chlorine is passed into acetaldehyde first at a low temperature, and afterwards at 100°, a substance named butylchloral is produced. Formation of this substance may most readily be understood if we imagine that the first action of the chlorine is to replace a single hydrogen atom in the aldehyde molecule and form monochlor-acetaldehyde—

$$CH_3.CO.H + Cl_2 = CH_2Cl.CO.H + HCl.$$

It will be remembered that aldehydes readily act with other substances, either by addition or with elimination of water. In this case we suppose that a molecule of chlor-acetaldehyde condenses with a molecule of acetaldehyde, water at the same

time being eliminated. The product of the reaction would be chloro-crotonic aldehyde, formed as follows :—

$$\underset{\text{Aldehyde}}{CH_3.CH:O} + \underset{\text{Chloraldehyde}}{H_2CCl.CO.H} = \underset{\text{Chloro-crotonic aldehyde}}{CH_3.CH:CCl.CO.H} + H_2O.$$

This being an unsaturated substance, combines with a molecule of chlorine and produces the so-called butylchloral—

$$CH_3.CH:CCl.CO.H + Cl_2 = \underset{\text{Butylchloral}}{CH_3.CHCl.CCl_2.CO.H}.$$

Like chloral, butylchloral or trichloro-butyric aldehyde combines readily with water to form an aldehydrol or hydrate. It crystallises well from water, in which it is moderately soluble, and is used in medicine as a hypnotic.

ACETIC ACID.

Acetic acid, $C_2H_4O_2$, is generally prepared from pyroligneous acid by first converting the crude acid into a salt, purifying this salt, and then liberating the acetic acid from it by means of a more powerful acid. It was stated above (p. 32) that in the preparation of methyl alcohol the vapours from the boiling pyroligneous acid were passed through warm milk of lime. The acetic acid contained in the pyroligneous acid vapours is converted by the milk of lime into calcium acetate, according to the equation—

$$2CH_3COOH + Ca(OH)_2 = (CH_3COO)_2Ca + 2H_2O.$$

If, when the lime is exhausted, the solution is evaporated to dryness, a crude calcium acetate is obtained. This salt is heated to about 250° to decompose and drive off any tarry matters with which it may be mixed, the salt itself not being decomposed at this temperature. If hydrochloric acid in quantity just insufficient to correspond to the calcium is now added, the acetic acid is liberated, according to the equation—

$$Ca(CH_3COO)_2 + 2HCl = CaCl_2 + 2CH_3.COOH,$$

and may be distilled off. The acetic acid obtained in this way is, of course, mixed with a considerable amount of water, which distils along with the acid. If a more concentrated acid is required, concentrated sulphuric acid may be used to liberate the acetic acid, in which case the distillation is best conducted

in a partial vacuum in order to reduce the temperature of distillation and to avoid charring of the organic matter by the concentrated sulphuric acid.

If it is not desired to prepare methyl alcohol from the pyroligneous acid, this acid may be neutralised at once with milk of lime or with crude sodium carbonate, and evaporated to dryness. The purification of the calcium or sodium salts is carried out as before, and the acetic acid liberated either by hydrochloric or sulphuric acid. To prepare practically anhydrous acetic acid, sodium acetate is fused to expel all water and tarry matter, and then decomposed by concentrated sulphuric acid at 120°.

Acetic acid prepared by the above method is extensively used in the dyeing industry, and for the preparation of numerous acetates of the metals and metallic radicals. It is employed in medicine in three states of dilution. The most concentrated is nearly pure acetic acid, containing 99 per cent. or over of the pure substance. It is known as *glacial* acetic acid, and freezes to a solid mass on a cold day. The common acetic acid of the pharmacopœia contains one-third of its weight of acetic acid, the other two-thirds being water. The dilute acetic acid contains a little over 4 per cent. acetic acid. Glacial acetic acid has a strong caustic action when applied to the skin, and is used for removing warts, etc.

Pure acetic acid is a colourless solid which melts at 16·7°, and possesses a characteristic, sharp, pungent odour. The liquid is slightly heavier than water, with which it mixes in all proportions. It boils at 118°, and the vapour burns with a bluish flame.

Acetic acid as an acid is much feebler than sulphuric, hydrochloric, or nitric acid, but still its acid properties are well marked, as even in dilute solution it possesses a sour taste, and readily acts on indicators such as litmus or phenolphthalein. It neutralises bases to form the acetates, and generally dissolves such metals as are soluble in dilute hydrochloric acid. As all the acetates are soluble, they are frequently employed both for chemical purposes and in the Pharmacopœia.

The acetates yield a red coloration with ferric chloride, due to the production of ferric acetate. When the red solution is boiled, a light-brown precipitate of basic ferric acetate

separates; and on addition of excess of hydrochloric acid to the red solution the red colour is discharged.

Production of Acetic Acid from Ethyl Alcohol.

It has been seen that the chief product of the oxidation of ethyl alcohol by chromic acid mixture is aldehyde, and that aldehyde is capable of further oxidation to acetic acid. It might be expected, therefore, that chromic acid mixture would oxidise ethyl alcohol to acetic acid directly. This oxidation does to a certain extent take place, but the aldehyde, which is the first oxidation product, for the most part escapes further oxidation by its great volatility. As soon as it is produced it leaves the solution containing the oxidising agent, and passes on as vapour into the condensing liquid.

Alcoholic liquids such as wine or beer are known to turn sour on exposure to air, the sourness being caused by the oxidation of the ethyl alcohol by means of atmospheric oxygen to acetic acid, through the agency of an enzyme. Pure ethyl alcohol even in dilute solution does not oxidise in this way, and may be left exposed indefinitely to the action of air or oxygen without turning sour. The difference between the two cases is, that the wine or beer contain in solution materials which act as food for certain bacteria which during their growth produce an enzyme which is capable of acting as a ferment in promoting the oxidation of ethyl alcohol by the oxygen of the air.

The process of this enzymatic oxidation of the ethyl alcohol contained in wine is carried out on a large scale industrially for the preparation of wine **vinegar.** The organism which effects the conversion of ethyl alcohol into acetic acid is a bacterium known as *Mycoderma aceti.* There are various methods of carrying out the process, only one of which need be indicated here. The wine which is to be oxidised is mixed with a little previously prepared vinegar, and allowed to trickle slowly over beech-wood shavings contained in a cask provided with a perforated false bottom on which the shavings rest, and with air-holes in the side of the cask near this false bottom, and also in its head. These air-holes are so regulated as to supply a slow but constant current of air in order that a sufficient amount of oxygen may be furnished for the oxidation. The

organism which effects the oxidation adheres to the shavings, and as the wine slowly trickles over them it meets with a current of air, and the conversion into acetic acid is slowly effected. It is necessary to run wine several times through such a cask before the alcohol is all oxidised. The process of oxidation is accelerated by the rise of temperature due to the heat liberated in the reaction. If the temperature rises above 40°, means must be taken to reduce it, as otherwise there is a considerable loss of material by volatilisation. A certain amount of aldehyde is formed and escapes during the oxidation, but if the process is working properly, 90 per cent. of the original alcohol may be converted into the corresponding quantity of acetic acid. The activity of the organism ceases when a concentration of about 14 per cent. of acetic acid has been reached in the solution, so that it is impossible by this process to prepare an acid of much more than 12 per cent. strength. Generally speaking, wine vinegar only contains about half that quantity of acetic acid, and owes its flavour, apart from the mere acidity, to the presence of other substances than alcohol originally contained in the wine. Malt vinegar is prepared in a similar way from alcoholic liquids produced by the fermentation of malt.

CHLORINE DERIVATIVES OF ACETIC ACID.

Chloracetic Acids.

The molecule of acetic acid contains four hydrogen atoms, only one of which is replaceable by metals. This hydrogen atom, which is a part of the carboxyl group, is not directly replaceable by chlorine, but the other three hydrogen atoms which form part of the hydrocarbon radical methyl can be replaced, as in a hydrocarbon itself, successively by chlorine atoms. The following equations illustrate the formation of the chloracetic acids from acetic acid:—

$$\underset{\text{Acetic acid}}{CH_3.COOH} + Cl_2 = \underset{\text{Monochloracetic acid}}{CH_2Cl.COOH} + HCl$$

$$\underset{\text{Monochloracetic acid}}{CH_2Cl.COOH} + Cl_2 = \underset{\text{Dichloracetic acid}}{CHCl_2.COOH} + HCl$$

$$\underset{\text{Dichloracetic acid}}{CHCl_2.COOH} + Cl_2 = \underset{\text{Trichloracetic acid}}{CCl_3.COOH} + HCl$$

The action of chlorine takes place most readily at the boiling-point of the liquid, and is assisted by the addition of a small quantity of iodine, which combines with the chlorine to form one of the chlorides of iodine, and these act as catalysts in the reaction. Monochloracetic and trichloracetic acids are solid at the ordinary temperature, whilst dichloracetic acid is a liquid. When trichloracetic acid is boiled with excess of alkali it is converted into sodium carbonate and chloroform, according to the equation—

$$CCl_3.COONa + NaOH = CHCl_3 + Na_2CO_3.$$

It will be observed that this action is analogous to the formation of methane by heating a mixture of sodium acetate and caustic soda, the chief difference being that it goes readily in aqueous solution. The analogy of the formation of chloroform from chloral, the corresponding aldehyde, may also be noted. The only difference is, that instead of potassium formate being obtained, as is the case with chloral, the second product of the reaction is here potassium carbonate.

Acetyl Chloride, $CH_3.CO.Cl$.

There is another chlorine derivative of acetic acid, namely, acetyl chloride, $CH_3.CO.Cl$, which must not be confused with chloracetic acid, $CH_2Cl.COOH$. In this compound the chlorine is not substituted for hydrogen, but for the hydroxyl group; it bears the same relation to acetic acid as ethyl chloride, C_2H_5Cl, bears to ethyl alcohol. It is produced by the action on acetic acid of phosphorus pentachloride, the equation being—

$$CH_3.CO.OH + PCl_5 = CH_3.CO.Cl + POCl_3 + HCl.$$

With regard to the constitution of this substance, it should be noted that the chlorine atom is attached directly to a carbon atom which is already oxidised. In chloracetic acid, on the other hand, the chlorine is attached to the carbon atom which is not oxidised. This difference of constitution corresponds to a great difference in properties. When a chlorine atom is attached to a non-oxidised atom, it is only with difficulty replaced by the hydroxyl group; but when a chlorine atom is attached to an oxidised carbon atom, the replacement of chlorine by hydroxyl takes place with great readiness. Chlor-

acetic acid may be boiled for a long time with water without reaction taking place to any great extent. Acetyl chloride, on the other hand, reacts with water readily at the ordinary temperature, with production of acetic acid and hydrochloric acid, thus—

$$\underset{\text{Acetyl chloride}}{CH_3.CO.Cl} + H_2O = \underset{\text{Acetic acid}}{CH_3.CO.OH} + HCl.$$

This reaction may be compared with the action of water on carbonyl chloride—

$$\underset{\text{Carbonyl chloride}}{COCl_2} + 2H_2O = \underset{\text{Carbonic acid}}{CO(OH)_2} + 2HCl.$$

Acetyl chloride is a liquid of low boiling-point, with a pungent odour, and fumes copiously in air owing to the action of the atmospheric moisture. It is a typical example of the substances known as **acyl chlorides.** Just as an alcohol radical or **alkyl** is derived from an alcohol by removing OH from the molecule—*e.g.* ethyl, C_2H_5, from ethyl alcohol, $C_2H_5.OH$—so an **acyl** is derived from an acid by abstracting hydroxyl from the molecule; so acetyl, $CH_3.CO$, from acetic acid, $CH_3.CO.OH$. The alkyl chlorides are not readily hydrolysed by water; the acyl chlorides are. In synthetic chemistry the acyl chlorides are much used on account of their great activity.

When acetyl chloride and anhydrous sodium acetate are warmed together the following reaction takes place:—

$$CH_3.CO.Cl + CH_3.CO.ONa = NaCl + \underset{\text{Acetic anhydride}}{(CH_3.CO)_2O}.$$

The substance $(CH_3CO)_2O$ is an oxide of the radical acetyl, and is the **anhydride** of acetic acid. When warmed with water, it is converted into acetic acid as follows:—

$$(CH_3.CO)_2O + H_2O = 2CH_3.CO.OH.$$

All the anhydrides proper of organic monobasic acids are similarly acyl oxides.

ESTERS AND SAPONIFICATION.

When an acid acts on a base with elimination of water, the substance produced is termed a salt. When an acid acts upon an alcohol with elimination of water, the substance produced is

termed an **ethereal salt** or **ester.** Between salts and esters there is little resemblance in physical properties, just as there is little resemblance between bases and alcohols. There is, however, a formal resemblance, in certain chemical actions in which these substances take part, of bases and salts on the one hand, to alcohols and esters on the other.

We have already met with examples of esters in the halogen compounds of the hydrocarbons. Thus, ethyl chloride is an ester according to the above definition, as it is formed from ethyl alcohol and hydrochloric acid with elimination of water—

$$C_2H_5OH + HCl = C_2H_5Cl + HOH.$$

Ethyl hydrogen sulphate is an acid ester corresponding to an acid salt, and may be formed from ethyl alcohol and sulphuric acid with elimination of water—

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + HOH.$$

These esters are examples of esters made by the interaction of an alcohol with an inorganic acid; but esters of organic acids are much more numerous, and are frequently prepared.

The common esters are generally volatile liquids possessing for the most part a pleasant odour, and it is to such esters that the fragrance of many flowers and fruits is due. They are, with few exceptions, either insoluble or sparingly soluble in water.

Whereas acids and bases react together almost instantaneously to produce salts, acids and alcohols react with each other very slowly to produce esters. Thus, if we mix acetic acid and ethyl alcohol in the proportions required by the following equation—

$$CH_3.COOH + C_2H_5OH \rightleftharpoons \underset{\text{Ethyl acetate}}{CH_3.COOC_2H_5} + HOH,$$

the action will go on slowly at the ordinary temperature, and even after a lapse of several years may not have reached the point of equilibrium. In order that the formation of ester may be accelerated it is usual to boil the alcohol and acid together in a vessel provided with a reflux condenser. The rise of temperature makes the reaction go much faster, but still it is comparatively slow. It is found, however, that the introduction of a comparatively small quantity of a strong mineral acid,

such as sulphuric acid or anhydrous hydrochloric acid, has a great catalytic influence, and the action then proceeds with sufficient rapidity. In the formation of the esters of hydrochloric and sulphuric acid the acids themselves act, not only directly in the action expressed by the equations (p. 84), but also as catalysts.

If we wish, then, to prepare ethyl acetate from ethyl alcohol and acetic acid, we add to the mixture of alcohol and acetic acid a small quantity of concentrated sulphuric acid, and heat the mixture to its boiling-point. The formation of ethyl acetate in this way is often used as a test both for ethyl alcohol and acetic acid. If it is desired, for example, to use it as a test for ethyl alcohol, a small quantity of acetic acid and some concentrated sulphuric acid are added to the liquid to be tested, and the mixture is then heated. If ethyl alcohol is present, the pleasant fruity odour of ethyl acetate, which is quite different from that of either ethyl alcohol or acetic acid, is soon perceived. **Ethyl acetate** is a colourless liquid of specific gravity 0·9 which boils at 77°. It is soluble in water to the extent of about 6 parts in 100.

The action leading to the formation of ethyl acetate is a reversible one, like all actions for the production of esters from alcohols and acids. If, therefore, we leave ethyl acetate in contact with water, the originally neutral ester slowly acquires an acid reaction owing to its resolution into ethyl alcohol and acetic acid—

$$CH_3.COOC_2H_5 + H_2O \rightleftharpoons CH_3.COOH + C_2H_5OH.$$

We have met with similar cases of hydrolysis in the action of water on the chlorine derivatives of methane. Like the formation of an ester, the **hydrolysis** of an ester by water is a slow process, but the same influences which accelerate the formation also accelerate the decomposition. We may therefore hydrolyse ethyl acetate rapidly by heating it to the boiling-point with water to which a little sulphuric acid or hydrochloric acid has been added.

Although esters may be hydrolysed directly in this way by means of water, they are more usually decomposed by means of an alkali. The product in such a case is not the acid itself, but an alkaline salt of the acid. For example, if ethyl acetate is

warmed with a solution of soda, it is rapidly decomposed with formation of sodium acetate and ethyl alcohol. The equation for this action is—

$$CH_3.COOC_2H_5 + NaOH = CH_3.COONa + C_2H_5OH.$$

It will be noticed that after this process of decomposition the ester or ethereal salt of the acid is converted into an ordinary metallic salt, the alkyl radical and the metallic radical changing places. As a result of this exchange, the hydroxyl group which was originally united with the metallic radical to form a base, is now united with the alkyl radical to form an alcohol. This process of converting an ethereal salt or ester into an alkaline salt is very frequently spoken of as **saponification** or soap-formation. The reason why this term is used is, that the natural animal and vegetable fats and oils are of the nature of esters, and when these are heated with alkalies, soaps and alcohols are produced. Since esters are commonly insoluble or sparingly soluble in water, alcohol is generally employed as a solvent, and the ester is saponified by means of an alcoholic solution of soda or potash.

As the number of organic acids is very great, and as the number of alcohols is also great, it is evident that the number of esters is still greater; for each acid can, theoretically at least, react with each alcohol to form an ester. This is in precise analogy with the number of salts derivable from the known acids and bases.

From the alcohols and organic acids with which we have already dealt, the following esters may be prepared:—

Methyl formate, $H.COOCH_3$, from formic acid, $H.COOH$, and methyl alcohol, $CH_3.OH$.

Ethyl formate, $H.COOC_2H_5$, from formic acid, $H.COOH$, and ethyl alcohol, $C_2H_5.OH$.

Methyl acetate, $CH_3.COOCH_3$, from acetic acid, $CH_3.COOH$, and methyl alcohol, $CH_3.OH$.

Ethyl acetate, $CH_3.COOC_2H_5$, from acetic acid, $CH_3.COOH$, and ethyl alcohol, $C_2H_5.OH$.

These are the simplest organic esters, and differ from most others in being comparatively soluble in water.

HOMOLOGOUS SERIES.

If we compare the formulæ of the three compounds, water, methyl alcohol, and ethyl alcohol, we find that these substances have in common the hydroxyl group—

Water	$H.OH$
Methyl alcohol	$CH_3.OH$
Ethyl alcohol	$C_2H_5.OH$

The presence of this common group is associated with certain definite chemical properties of the substances containing it. Thus these substances all react readily with sodium, hydrogen being evolved, and the sodium compounds—

$H.ONa$	Sodium hydroxide
$CH_3.ONa$	Sodium methoxide
$C_2H_5.ONa$	Sodium ethoxide

being produced. Again, phosphorus trichloride gives with the three substances the following compounds:—

HCl	Hydrogen chloride
CH_3Cl	Methyl chloride
C_2H_5Cl	Ethyl chloride

If we now compare the radicals which we find repeated in these sets of compounds, we see that they are respectively H, CH_3, and C_2H_5. We can derive CH_3 from H by the addition of CH_2, and similarly C_2H_5 from CH_3 by the addition of CH_2. Now if we suppose this process to be repeated, starting from C_2H_5 we can obtain by addition of CH_2 the radical C_3H_7, and from this in succession by a repetition of the process the radicals C_4H_9, C_5H_{11}, C_6H_{13}, C_7H_{15}, and so on. Now, such radicals are actually found in organic compounds, and we may extend the

list of alcohols, *i.e.* their compounds with OH, so as to include them—

		B. Pt.	Δ.
Methyl alcohol .	. $CH_3.OH$	57°	22
Ethyl alcohol .	. $C_2H_5.OH$	78°	24
Propyl alcohol .	. $C_3H_7.OH$	102°	22
Butyl alcohol .	. $C_4H_9.OH$	124°	24
Amyl alcohol .	. $C_5H_{11}.OH$	148°	21
Hexyl alcohol .	. $C_6H_{13}.OH$	169°	22
Heptyl alcohol .	. $C_7H_{15}.OH$	191°	

These alcohols have all been prepared and exhibit similar chemical properties. For example, they all act upon sodium with production of hydrogen and an alkoxide; they all react with phosphorus trichloride with production of an alkyl chloride. The term **alcohol radical** or **alkyl** is used to denote any of the preceding radicals which combine with hydroxyl to form an alcohol.

When we compare the properties of the alcohols in such a series, which is known as a **homologous series**, we find that they generally show a regular variation. Thus, as the series is ascended—that is, as the number of atoms in the molecule increases—we find that the boiling-points rise, as reference to the preceding table will show. This is not only the case for the alcohols, but for all homologous series of the same type. The **alkyl chlorides**, for example, show the following boiling-points:—

CH_3Cl .	. Methyl chloride	− 24°	
C_2H_5Cl .	. Ethyl chloride	+ 12°	36
C_3H_7Cl .	. Propyl chloride	46°	34
C_4H_9Cl .	. Butyl chloride	78°	32
$C_5H_{11}Cl$.	. Amyl chloride	107°	29
$C_6H_{13}Cl$.	. Hexyl chloride	133°	34
$C_7H_{15}Cl$.	. Heptyl chloride	159°	26

In addition to this gradation in physical properties there exists a similar gradation in chemical properties. It has already been said that sodium acts upon all the alcohols with expulsion of hydrogen. The ease, however, with which the sodium acts depends very much on the position of the alcohol in the homologous series. Sodium and methyl alcohol react

almost as vigorously as sodium and water. With ethyl alcohol the action is not quite so vigorous, and as the series is ascended the action becomes less and less brisk, until with heptyl alcohol, $C_7H_{15}.OH$, the action is quite sluggish.

Of the above alcohols it is only methyl and ethyl alcohol that are of much (more) importance. Butyl and amyl alcohols are formed to a small extent in the fermentation of sugar by yeast. Owing to their higher boiling-points they are comparatively easily separated from ethyl alcohol.

The alcohols and the alkyl chlorides are frequently looked upon as derivatives of hydrocarbons. These hydrocarbons are of little importance in themselves in a pure state, but from a systematic point of view it is often necessary to refer to them. The following table contains the names of the simpler **saturated hydrocarbons**, together with the names of the corresponding univalent hydrocarbon radicals, or **alkyls**, derived from them by abstraction of one atom of hydrogen. It should be noted that this abstraction of hydrogen from a hydrocarbon is purely an ideal process, and that alkyls can lead no independent existence, but merely appear as components of more complex molecules :—

Saturated Hydrocarbon.		Alkyl.	
CH_4	Methane	CH_3	Methyl
C_2H_6	Ethane	C_2H_5	Ethyl
C_3H_8	Propane	C_3H_7	Propyl
C_4H_{10}	Butane	C_4H_9	Butyl
C_5H_{12}	Pentane	C_5H_{11}	Amyl
C_6H_{14}	Hexane	C_6H_{13}	Hexyl
C_7H_{16}	Heptane	C_7H_{15}	Heptyl
C_8H_{18}	Octane; etc.	C_8H_{17}	Octyl; etc.

The names of the alkyls correspond to the names of the saturated hydrocarbons, the termination *ane* of the saturated hydrocarbons being replaced by the termination *yl* for the alkyls. The only exception is in the case of pentane, which gives rise to an alkyl which retains the older name of amyl instead of the strict systematic name of pentyl. The names of higher hydrocarbons and alkyls than those given in the table are derived in a similar way from the Greek numerals.

If we consider the formulæ of the hydrocarbons we find that

in each member of the series the number of hydrogen atoms is equal to twice the number of carbon atoms with two hydrogen atoms in addition. We may, therefore, write a **general formula** to express the composition of all the saturated hydrocarbons by making use of this relation. This general formula is C_nH_{2n+2}. If for n we substitute the numerals 1, 2, 3, etc., in order, we obtain the formulæ of all possible saturated hydrocarbons. Similarly, we may write for the alkyls the general formula C_nH_{2n+1}, for the alkyl chlorides the general formula $C_nH_{2n+1}Cl$, and for the alcohols $C_nH_{2n+1}OH$. By using these general formulæ it is possible to write general equations illustrating the action of a certain reagent, not on a single substance only, but on the whole homologous series to which the substance belongs. Thus we can write a general equation for the action of phosphorus trichloride on the alcohols as follows:—

$$3C_nH_{2n+1}OH + PCl_3 = 3C_nH_{2n+1}Cl + H_3PO_3.$$

It will be noticed that as the value of n increases the proportion which the hydrocarbon radical bears to the element or group of elements with which it is united increases also. One effect of this in determining the properties of the members of homologous series may be illustrated by considering the solubility of the various alcohols in water. The hydrocarbons themselves are practically insoluble in water, and therefore we should expect a compound in which the hydrocarbon portion largely predominates would resemble the hydrocarbon itself in this respect. On the other hand, the presence of the hydroxyl group OH in an organic substance tends to make that substance soluble in water, which itself is chiefly composed of the hydroxyl group. We might expect, then, that the solubility of the alcohols in water would diminish as the homologous series is ascended—that is, as the proportion of hydroxyl to hydrocarbon diminishes; this we find to be the case. Methyl alcohol, ethyl alcohol, and propyl alcohol mix with water in all proportions. Butyl alcohol at the ordinary temperature has a solubility of only 30 parts in 100, amyl alcohol 6 parts, and alcohols like octyl alcohol are scarcely soluble in water at all. But as liquids of similar nature generally dissolve each other, we might expect those alcohols which have large hydrocarbon radicals to be soluble in the

liquid hydrocarbons. We actually find that whilst methyl alcohol, in which the proportion of hydrocarbon is not great, is very little soluble in pentane, the higher alcohols such as octyl alcohol mix freely with this hydrocarbon.

When an alkyl radical is combined with the radical carboxyl COOH, the resulting substance is an acid. The series of acids thus obtained is known as the series of saturated **fatty acids**, for acids which occur in the form of esters in animal and vegetable fats and oils belong to it.

The following table gives the names and formulæ of some of the principal fatty acids, all of which may be expressed by the general formula $C_nH_{2n+1}.COOH$:—

$H.COOH$	Formic acid
$CH_3.COOH$	Acetic acid
$C_2H_5.COOH$	Propionic acid
$C_3H_7.COOH$	Butyric acid
$C_4H_9.COOH$	Valeric acid
$C_5H_{11}.COOH$	Caproic acid
.	.
.	.
.	.
.	.
$C_{15}H_{31}.COOH$	Palmitic acid
.	.
$C_{17}H_{35}.COOH$	Stearic acid

The two acids last mentioned in the table are these found in the fats and oils. It will be noticed that in them the proportion borne by the hydrocarbon group to the hydroxyl group is very large, and we find that in consequence these acids are practically insoluble in water, unlike the first acids of the series, formic acid and acetic acid, which mix with water in all proportions.

If the alkyl radical is combined with the aldehyde group, $CO.H$, the homologous series of the **fatty aldehydes** is obtained. They differ from the acids in having one oxygen atom less in the molecule, and their names are derived from the names of the corresponding acids. Thus the series begins with formic aldehyde or formaldehyde, $H.CO.H$, acetic aldehyde, $CH_3.CO.H$, propionic aldehyde, $C_3H_7.CO.H$, etc.

GRAPHIC FORMULÆ AND ISOMERISM.

It has already been indicated that in the graphic or constitutional formula of the carbon compounds containing oxygen and hydrogen, that hydrogen is always represented as a monad element, oxygen as a dyad element, and carbon as a tetrad element. So long as the compounds considered are simple, there is generally only one way of joining the atoms so that each retains its proper valency. For example, it is impossible to write any other formula than

$$\begin{array}{ccccccc} & & H & & & & \\ & & | & & & & \\ H & — & C & — & O & — & H \\ & & | & & & & \\ & & H & & & & \end{array}$$

for methyl alcohol. If, on the other hand, we try to write the graphic formula for the compound C_2H_6O, we find that two formulæ are possible, namely :—

$$\begin{array}{ccccccccc} & & H & & H & & & & \\ & & | & & | & & & & \\ H & — & C & — & C & — & O & — & H \\ & & | & & | & & & & \\ & & H & & H & & & & \\ & & & \text{I.} & & & & & \end{array} \qquad\qquad \begin{array}{ccccccccc} & & H & & & & H & & \\ & & | & & & & | & & \\ H & — & C & — & O & — & C & — & H \\ & & | & & & & | & & \\ & & H & & & & H & & \\ & & & & \text{II.} & & & & \end{array}$$

In each of these the elements appear with their proper valency, and so the system of symbolisation would point to the possible existence of two compounds having the formula C_2H_6O. Now, two such compounds are known to exist, and these have received the names of ethyl alcohol and methyl ether. They are quite different in their physical and chemical properties; methyl ether, for example, being a gas at ordinary temperatures,

whilst ethyl alcohol is a liquid which boils at 78°. Our system of writing formulæ, then, is so far justified, but there still remains the problem as to which of the two possible formulæ is to be given to ethyl alcohol, and which to methyl ether.

A consideration of the two formulæ will indicate the lines on which chemists proceed in order to determine questions of this nature. In formula II. all the hydrogen atoms bear exactly the same relation to the whole molecule. In formula I., on the other hand, one of the hydrogen atoms is different from the others, because it is combined directly with oxygen, whereas the others are combined directly with carbon. We may expect, then, some indication of this difference of one hydrogen atom from the others in the chemical properties of the substance which this formula would represent. We find such a difference in the case of ethyl alcohol. When ethyl alcohol is brought into contact with sodium, one of the six hydrogens is replaced by sodium, with formation of the compound C_2H_5ONa. Again, when ethyl alcohol reacts with hydrochloric acid, a substance of the formula C_2H_5Cl is formed. One hydrogen here has left the molecule along with an atom of oxygen, and the place of these two has been taken by an atom of chlorine. It is reasonable to suppose, then, that in the molecule of ethyl alcohol this hydrogen has been associated with the oxygen atom, whereas the other five hydrogens are associated with carbon; because in ethyl chloride, the product of the reaction, they still remain associated with carbon, for there is only one way of writing the graphic formula of ethyl chloride, namely:—

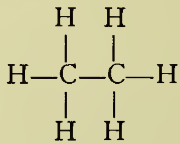
$$
\begin{array}{ccccccc}
 & & \mathrm{H} & & \mathrm{H} & & \\
 & & | & & | & & \\
\mathrm{H} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{Cl} \\
 & & | & & | & & \\
 & & \mathrm{H} & & \mathrm{H} & &
\end{array}
$$

Methyl ether, on the other hand, reacts neither with sodium with formation of a compound C_2H_5ONa, nor with hydrochloric acid with formation of a compound C_2H_5Cl.

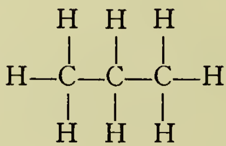
From these considerations alone it would be justifiable to assign formula I. to ethyl alcohol, and formula II. to methyl ether. This conclusion is confirmed by the whole chemical behaviour of the two substances. Methyl ether never acts as

if it contained a hydroxyl group; ethyl alcohol always acts as if this group were present.

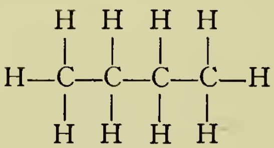
If we attempt to write the graphic or constitutional formula of the hydrocarbon ethane, we find that this can be done in only one way—



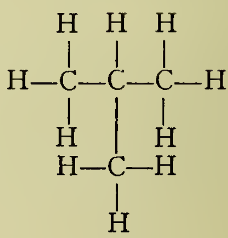
Similarly, there is only one possible formula for the hydrocarbon propane, C_3H_8, namely :—



When, however, we come to the hydrocarbon butane, there are two possible formulæ, namely :—



Butane



Isobutane

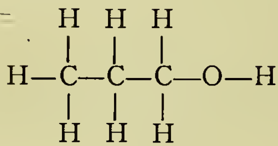
Now if our system of symbolisation is a good one, the number of actually existing substances ought to correspond with the number of possible formulæ. This requirement is fulfilled; only one substance is known of the formula C_2H_6, only one with the formula C_3H_8, but two substances exist which have the formula C_4H_{10}. One of these is known as normal butane, the other as isobutane. In normal butane we have what is termed a straight carbon chain, that is, a chain in which each carbon is directly united to not more than two other carbon atoms. In isobutane a branched chain

occurs, one of the four carbon atoms being linked directly to three others.

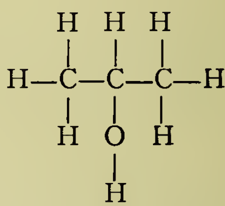
As the number of carbon atoms in a hydrocarbon increases, the possibility of obtaining different substances of the same molecular formula increases still more rapidly; but it is to be noted that there is a general correspondence between the number of graphic formulæ for a given empirical formula and the number of actual substances possessing that empirical formula. Substances which have the same empirical molecular formula but different constitutional or graphic formulæ are said to be **isomeric** (p. 23).

CLASSIFICATION OF ALCOHOLS.

The isomerism among the alcohols offers some points of considerable importance. If we endeavour to write the formula of propyl alcohol, $C_3H_7.OH$, arranging the symbols so that it shall contain the hydroxyl group which is found in all alcohols, we find that there are two possible methods of constructing the graphic formulæ—



Propyl alcohol

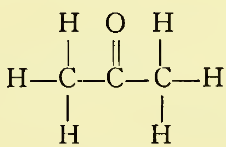


Isopropyl alcohol

In one of these formulæ the hydroxyl group is attached to a terminal carbon atom, in the other it is attached to the intermediate carbon atom. Corresponding to these two formulæ, two propyl alcohols are actually known: one the ordinary propyl alcohol, which boils at 97°; the other isopropyl alcohol, which boils at 81°. It will be noticed that formula I. contains the grouping CH_2OH, whereas formula II. does not. According to what has been stated, the group CH_2OH is characteristic of what we term **primary alcohols**, and is converted by oxidation, first into the aldehyde group $CO.H$, and then into the carboxyl group $COOH$. One of the propyl alcohols therefore should, on oxidation, yield an aldehyde and then an acid, and this alcohol should contain the primary alcohol group CH_2OH; that is, it should be represented by formula I. Propyl alcohol, on oxidation, yields propionic

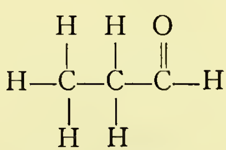
aldehyde, $C_2H_5.CO.H$, and propionic acid, $C_2H_5.CO.OH$. We may safely, therefore, attribute to it formula I.

Isopropyl alcohol contains the group $>$CH.OH or CH(OH) which is characteristic of what we term **secondary alcohols.** By oxidation these alcohols lose two atoms of hydrogen and become converted, not into aldehydes, which contain the group CO.H, but into ketones which contain the group CO, this group being combined with carbon atoms on both sides. Thus, when isopropyl alcohol is oxidised it gives rise to the ketone $CH_3.CO.CH_3$, which is termed acetone, and may be represented graphically by the formula—



Acetone

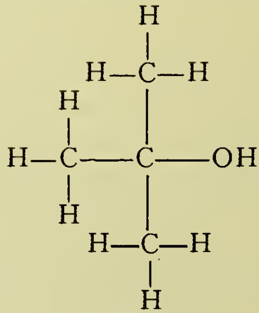
This ketone is isomeric with propionic aldehyde, which is obtained by oxidation from ordinary propyl alcohol. The graphic formula of propionic aldehyde is—



Propionic aldehyde

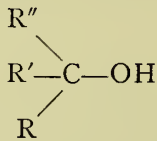
There is still another class of alcohols which are named **tertiary alcohols.** In these the hydroxyl group is united to the carbon atom, which in its turn is only united to other carbon atoms. The alcohols thus contain the group $\gtrdot$C.OH. These tertiary alcohols cannot, like the primary and secondary alcohols, lose two atoms of hydrogen by oxidation. They give rise to neither aldehydes and acids, like the primary alcohols, nor to ketones, like the secondary alcohols. They are either not attacked by oxidising agents at all, or if attacked are split up into simpler molecules, that is, molecules

containing a smaller number of carbon atoms. The graphic formula of the simplest tertiary alcohol is—



Tertiary butyl alcohol

If we indicate by R any univalent alcohol radical, then all primary alcohols have the formula $RCH_2.OH$, and in this group we also include methyl alcohol, the simplest of all alcohols, which has a hydrogen atom instead of the alkyl group R. Secondary alcohols may be indicated in the same way by the formula $R.CH(OH).R'$, in which R and R′ may either be the same or different alkyls. Tertiary alcohols, finally, are indicated by the formula—



Using this abbreviated method of indicating constitutional formulæ, we may write that of propyl alcohol as follows, $CH_3.CH_2.CH_2.OH$, that of isopropyl alcohol, $(CH_3)_2CH.OH$, and that of tertiary butyl alcohol, $(CH_3)_3C.OH$.

During the alcoholic foundation of sugar by yeast there is produced not only ethyl alcohol, but a mixture of higher boiling alcohols which are contained in the fusel oil which is separated in the course of rectification. The chief of these **fusel oil alcohols** are—

Normal propyl alcohol	$C_2H_5.CH_2.OH$
Isobutyl alcohol	$(CH_3)_2CH.CH_2.OH$
Isoamyl alcohol	$(CH_3)_2CH.CH_2.CH_2.OH$
Optically active amyl alcohol	$(CH_3.CH_2)(CH_3)\mathbf{C}H.CH_2.OH$

It will be noted that all these alcohols of fermentation are primary alcohols.

If we look upon the alcohols as mono-substitution products of the hydrocarbons, derived from the parent hydrocarbons by substitution of the hydroxyl group for one hydrogen atom, it is evident that the number of isomeric alcohols will always be the same as the number of isomers of any other mono-substitution product. For example, if we consider the monochloro-derivatives of the hydrocarbons, we see that there must be one and only one corresponding to each alcohol, for the monochloro-derivative is related to the corresponding alcohol by the substitution of an atom of chlorine for the hydroxyl group, which substitution can always be effected practically by means of one of the chlorides of phosphorus. Similarly, if for the hydroxyl group of the alcohols we suppose the aldehyde group $CO.H$, or the acid group $COOH$, to be substituted, we derive the complete series of the isomeric aldehydes and of the isomeric acids; and so it is for all other mono-substitution derivatives of the hydrocarbons.

As has already been indicated, the number of possible isomers for the higher terms of homologous series is very great, and many of these have been prepared artificially. In nature, however, there is a tendency to the formation of certain restricted types of compounds. For example, there seems to be a tendency to the formation of long, straight, unbranched chains. The acids from the natural fats, palmitic acid, $C_{15}H_{31}.COOH$, and stearic acid, $C_{17}H_{35}.COOH$, are straight chain compounds. Most of the saturated hydrocarbons found in natural paraffin oils, and also the natural sugars, are straight chain compounds. Exceptions to this rule, however, occur, as may be seen above in the formulæ of the higher alcohols of fermentation.

KETONES.

Ketones are compounds of the general type $R.CO.R'$, in which R and R' represent two hydrocarbon radicals which may either be the same or different. The simplest ketone is acetone, $CH_3.CO.CH_3$, which may be taken as a typical example of the whole class.

Ketones in many respects resemble aldehydes in their behaviour, but they differ from aldehydes in having no reducing properties. The reducing properties of aldehydes depend upon the possibility of the conversion of the aldehyde R.CO.H into the corresponding acid R.CO.OH. No such oxidation is possible in the case of ketones, so that they are without reducing action. The ketones react with hydroxylamine and with phenylhydrazine as aldehydes do, with formation of oximes and phenylhydrazones, in accordance with the equations—

$$\begin{matrix}R\\R'\end{matrix}\!\!>CO + H_2N.OH = \begin{matrix}R\\R'\end{matrix}\!\!>C:NOH + H_2O$$

$$\begin{matrix}R\\R'\end{matrix}\!\!>CO + H_2N.NHC_6H_5 = \begin{matrix}R\\R'\end{matrix}\!\!>C:N.NHC_6H_5 + H_2O$$

Just as aldehydes may be formed from primary alcohols, and on reduction be reconverted into these alcohols, so ketones may be formed by the oxidation of secondary alcohols, and may be reconverted into these secondary alcohols by reduction. Ketones, unlike aldehydes, show no tendency to polymerisation.

Acetone, $CH_3.CO.CH_3$.

It has already been stated that acetone is one of the products of the distillation of wood, and occurs in consequence as a normal impurity in crude methyl alcohol. Acetone is also found in small quantities in the human body, especially in certain diseased conditions. It is generally prepared by the dry distillation of calcium acetate. When this substance in the dry state is heated in a tube at a moderately high temperature in absence of air, the calcium acetate decomposes with production of calcium carbonate and acetone, according to the following equation—

$$(CH_3.COO)_2Ca = CaCO_3 + CH_3.CO.CH_3.$$

At the temperature of decomposition the acetone passes off as vapour, together with certain other higher-boiling products, and is condensed along with them to the liquid state. When the crude liquid thus obtained is redistilled, the acetone passes

over at a low temperature, and may be further purified by converting it into a crystallisable addition compound with sodium hydrogen sulphite. This addition compound is exactly similar to the corresponding bisulphite compounds formed from aldehydes. On warming with alkali it is decomposed, and the acetone is expelled. The acetone has then only to be freed from any water with which it is still mixed, to be perfectly pure. It is finally distilled over quicklime or calcium chloride.

Acetone is a colourless liquid with a characteristic, not unpleasant, odour. It has a specific gravity of about 0·8, and boils at 56°. It mixes in all proportions with water, alcohol, and ether, and is used as a solvent for fats, resins, nitro-cellulose, etc.

Although it does not act as a reducing agent in the ordinary sense, it is capable of being oxidised by powerful oxidising agents. Thus, potassium bichromate and sulphuric acid oxidise it to acetic acid and formic acid, according to the equation—

$$CH_3.CO.CH_3 + 3(O) = CH_3.COOH + H.COOH,$$

and the formic acid may be further oxidised to carbonic acid. This process of oxidation is entirely different from the oxidation of an aldehyde to the corresponding acid. In the case of the aldehyde the carbon chain remains unbroken; in the case of acetone the carbon chain is split into two portions, one containing two carbon atoms and one containing a single carbon atom.

Acetone, like ethyl alcohol, gives iodoform on treatment with iodine and an alkali, and may be used as a source of iodoform. It is also used commercially as a source of chloroform, which may be prepared from it by precisely the same method as is used in the case of ethyl alcohol. The action of bleaching powder on acetone gives rise by chlorination to trichloroacetone, $CCl_3.CO.CH_3$. This substance, like trichloroaldehyde, is decomposed by alkalies, with production of chloroform and an acetate of the alkali. For comparison, the equations representing the action of caustic soda on trichloroaldehyde and on trichloroacetone are given below:—

$$CCl_3.CO.H + NaOH = CCl_3H + H.COONa$$
$$CCl_3.CO.CH_3 + NaOH = CCl_3H + CH_3.COONa$$

THE SATURATED HYDROCARBONS.

MINERAL OILS AND WAXES.

We have seen that the simplest of the saturated hydrocarbons, marsh gas or methane, CH_4, is a natural product. It not only occurs in marshes as a product of vegetable decay, and in the atmosphere of coal-mines as fire-damp, but also as a general constituent of natural gas, which may be obtained in certain regions by boring—for example, at Pittsburg in America and Salsomaggiore in Italy. The next member of the series of saturated hydrocarbons, ethane, C_2H_6, occurs in these natural gases in smaller quantity, and the higher members of the series are found mixed with each other in liquid petroleum and solid paraffin wax.

The general regions in which petroleum is found are Pennsylvania, Mexico, Baku on the Caspian Sea, and Galicia (Austrian Poland). The oil is obtained from oil-wells, which resemble in main features ordinary deep wells for water. Sometimes, when a fresh bore is sunk, the oil not only rises to the surface, but spouts up in the form of a fountain. Generally, however, it is necessary, as in the case of water, to force the oil up to the surface. The chief constituents of the American oils are hydrocarbons of the saturated series C_nH_{2n+2}, mixed with smaller quantities of unsaturated hydrocarbons. The Russian oils, on the other hand, contain chiefly hydrocarbons of the so-called naphthene series, the general formula for which is C_nH_{2n}. Every saturated hydrocarbon from CH_4 to $C_{27}H_{56}$ has been found in the American oils, and these hydrocarbons have all the normal or straight carbon chain constitution.

Crude **petroleum** is an oily liquid of specific gravity about 0·8, although there is considerable variation in this respect according to the district. The liquid is usually of a dark colour, varying from greenish or reddish brown to nearly black. It contains, dissolved in it, the lower gaseous members of the series of saturated hydrocarbons or paraffins. The name **paraffin** was given to the hydrocarbons of this series on account of the feeble affinity which they exhibit—that is, to the difficulty

which is experienced in acting on them by means of the ordinary chemical reagents.

In order to separate the various constituents of the crude oil, it is subjected to fractional distillation. No attempt is made to separate the individual hydrocarbons, but merely to group them according to their volatility into fractions which are suited to some practical end. Starting with the most volatile substances, we have the following groups—

(1) Solvent naphthas and petrols; (2) illuminating oils; (3) lubricating oils; (4) solid and semisolid paraffins; (5) a residue of paraffin coke.

The most volatile fractions of the first group are used principally as solvents for fats, etc., the name **petroleum ether** being applied to those boiling at about 50°. Those boiling at about 75° are largely used as **petrol** for motors, as well as for solvent purposes. The **illuminating oils** are much less volatile, since otherwise there is great liability to explosion in the lamps. Generally speaking, the boiling-point of these mixtures used for lamps should be in the neighbourhood of the boiling-point of mercury, namely 360°. The **lubricating oils** are more viscid than the paraffin used for illuminating purposes, and constitute the next important fraction of the crude petroleum. Still higher-boiling fractions are semisolid at the ordinary temperature, and are known as **petroleum jelly**, **vaseline**, etc. These are used as bases for ointments and the like. Hard paraffin or **paraffin wax** forms the highest boiling fraction of the products of distillation of paraffin. At the ordinary temperature paraffin wax is a comparatively hard, crystalline substance, slightly greasy to the touch. It is sold in different grades according to its melting-point, which may range from 35° to 60°. These paraffin waxes are much used in imbedding tissues which are to be cut for microscopic sections, and in the manufacture of candles. **Ozokerite**, or earth wax, is a hard paraffin occurring naturally in Poland. From it is prepared **ceresin**, which melts at about 55°.

As has already been mentioned, these hydrocarbons, although useful for many purposes, do not serve as points of departure for the preparation of other chemical substances, and therefore need not be further considered.

ORGANIC SOLVENTS.

The following list contains the solvents commonly employed for the solution of organic substances :—

		B. Pt.
Water . . .	H_2O	100° C.
Methyl alcohol . .	$CH_3.OH$	66°
Ethyl alcohol . .	$C_2H_5.OH$	78°
Acetone . .	$CH_3.CO.CH_3$	56°
Ethyl ether . .	$C_2H_5.O.C_2H_5$	35°
Chloroform . .	$CHCl_3$	61°
Benzene . .	C_6H_6	80°
Petroleum ether .	C_5H_{12}; etc.	50°

It will be observed that these are all neutral substances, and that they have comparatively low boiling-points, so that they may be easily removed by evaporation.

The solvents are arranged in order of resemblance to each other in their solvent action.

As extremes, we have water on the one hand, a saturated hydrocarbon on the other. Water is, generally speaking, used to dissolve salts and substances containing a large proportion of the hydroxyl group (or certain nitrogenous groups) in the molecule. It is not in general a good solvent for substances containing large hydrocarbon groups, or such groups in which hydrogen has been replaced by chlorine or other halogen. Thus water dissolves freely the alkaline salts of organic acids, the chlorides of organic bases, substances such as glycerol, $C_3H_5(OH)_3$, pyrogallol, $C_6H_3(OH)_3$, the sugars, etc. It does not dissolve to any marked extent paraffins, chloroparaffins (*e.g.* chloroform, which is only very slightly soluble), or the fats and oils.

The hydrocarbon solvents, on the other hand, easily dissolve solid paraffins, oils, and fats, but not glycerol, or the salts of organic acids. Ethyl ether and chloroform may, on the whole, be grouped with the hydrocarbon solvents, and are frequently used in the extraction of fats.

In a homologous series, such as that of the alcohols or fatty acids, we find that the lower members, which have a large proportion of the group OH or COOH, are freely soluble

in water, whereas the higher members, in which the hydrocarbon radical is preponderant, are almost insoluble in water, but soluble in hydrocarbons.

Methyl alcohol and ethyl alcohol show some resemblance to water, especially the former, but they both dissolve many substances which are practically insoluble in water. Acetone bears a general resemblance to them in its properties.

If we consider a liquid such as glycerol, $C_3H_5(OH)_3$, we find that it mixes freely with water, the alcohols, and acetone; but that it is only sparingly soluble in ether, and practically insoluble in chloroform and the hydrocarbon solvents.

The fats, again, which are readily soluble in ether, and the solvents following it in the list, are only moderately soluble in acetone and the alcohols, and are practically insoluble in water.

Water itself mixes in all proportions with methyl and ethyl alcohol, and with acetone; it is only partially miscible with ether, and nearly immiscible with chloroform and the hydrocarbons. Petroleum ether mixes with all the solvents enumerated except water, with which it is nearly immiscible, and methyl alcohol, with which it is only partially miscible.

A good example of the use of solvents is afforded by the process of imbedding tissues in paraffin for the purpose of cutting microscopic sections. The tissues are normally bathed in an aqueous fluid, and the object is to replace this water by melted paraffin wax, which will set on cooling, and permit the specimen to be cut into thin sections for the microscope.

It is impossible to displace the water by melted paraffin directly, since the two liquids are immiscible. The specimen is therefore soaked in ethyl alcohol of increasing concentration, finally in absolute alcohol. The water is in this way dissolved out, and replaced by alcohol. The next process is to replace the alcohol by chloroform, or some liquid hydrocarbon (dimethylbenzene or xylene, C_8H_{10}, is most frequently employed), by soaking the specimen in this new solvent. Finally, when the specimen is fully charged with xylene, say, it may be immersed in a bath of melted paraffin wax, which gradually replaces the xylene, with which it mixes freely.

Besides the neutral substances mentioned above, basic substances such as pyridine, and acid substances such as acetic

acid, are occasionally used as solvents. Their use is, however, limited by the fact that there are large classes of substances with which they act chemically to form stable compounds.

ANIMAL AND VEGETABLE OILS, FATS, AND WAXES.

As we have seen, the mineral oils consist of mixtures of hydrocarbons. The fixed animal and vegetable oils, on the other hand, consist essentially of esters, so that they contain a certain proportion of oxygen as well as carbon and hydrogen. The chief acids which go to form these esters are the two saturated fatty acids, **palmitic acid**, $C_{15}H_{31}COOH$, and **stearic acid**, $C_{17}H_{35}COOH$, together with the unsaturated acid **oleic acid** $C_{17}H_{33}COOH$. The chief alcohol from which the esters are derived is the triatomic alcohol **glycerol**, $C_3H_5(OH)_3$.

We have so far dealt only with the monohydric alcohols, that is, alcohols containing a single OH group. These correspond to the monacid bases, *e.g.*, caustic soda, NaOH, or ammonium hydroxide, NH_4OH; but just as we have diacid and triacid bases, such as calcium hydroxide, $Ca(OH)_2$, and aluminium hydroxide, $Al(OH)_3$, so we have dihydric alcohols, *e.g.*, glycol, $C_2H_4(OH)_2$, and trihydric alcohols, such as glycerol, $C_3H_5(OH)_3$. The base aluminium hydroxide is capable of reacting with three molecules of a monobasic acid, for example, acetic acid, according to the following equation :—

$$Al(OH)_3 + 3CH_3.COOH = (CH_3.COO)_3Al + 3H_2O.$$

Similarly the trihydric alcohol glycerol is capable of acting with three molecules of a monobasic acid to form an ester—

$$C_3H_5(OH)_3 + 3CH_3.COOH = \underset{\text{Glyceryl acetate}}{(CH_3.COO)_3C_3H_5} + 3H_2O.$$

The triad radical C_3H_5 of glycerol is termed glyceryl, so that the ester derived from glycerol and acetic acid may be termed glyceryl acetate. Now, if instead of acetic acid we take palmitic acid, stearic acid, or oleic acid, and produce their esters with glycerol, we obtain the substances glyceryl tripalmitate,

glyceryl tristearate, and glyceryl trioleate, in the manner represented by the following equations :—

$$C_3H_5(OH)_3 + 3C_{15}H_{31}.COOH = (C_{15}H_{31}.COO)_3C_3H_5 + 3H_2O$$

Glyceryl tripalmitate

$$C_3H_5(OH)_3 + 3C_{17}H_{35}.COOH = (C_{17}H_{35}.COO)_3C_3H_5 + 3H_2O$$

Glyceryl tristearate

$$C_3H_5(OH)_3 + 3C_{17}H_{33}.COOH = (C_{17}H_{33}.COO)_3C_3H_5 + 3H_2O$$

Glyceryl trioleate

These esters are the chief constituents of the vegetable and animal oils and fats. The saturated esters glyceryl tripalmitate or **tripalmitin** and glyceryl tristearate or **tristearin** are solid at the ordinary temperature. Glyceryl trioleate or **triolein**, on the other hand, is liquid at the ordinary temperature. Tripalmitin, tristearin, and triolein almost invariably occur associated together. If the tripalmitin and tristearin predominate, the mixture is solid at the ordinary temperature, and is termed a **fat**. If the triolein preponderates, the mixture is liquid at the ordinary temperature, and is termed an **oil**. These oils, owing to their complexity, have a high boiling-point and are not volatile without decomposition, so that they are spoken of as the fixed or non-volatile oils, in contradistinction to the essential or volatile oils, which have a comparatively low boiling-point.

Milk fat differs from the other fats and oils by containing, combined with glycerol, a considerable proportion of fatty acids, *e.g.* butyric and caproic acids (p. 91), which are lower in the series than palmitic acid.

The fats and oils, since they are, chemically speaking, esters, may like other esters be hydrolysed and split up into the corresponding alcohol and acid. Thus, if we hydrolyse tristearin, we obtain the alcohol glycerol and stearic acid, according to the equation—

$$C_3H_5(C_{17}H_{35}.COO)_3 + 3H_2O = C_3H_5(OH)_3 + 3C_{17}H_{35}.COOH.$$

The hydrolysis may be effected by means of water alone at a high temperature (superheated steam), but the action may be greatly accelerated by the addition of a small quantity of acid.

In the animal body the hydrolysis is effected by a fat-splitting enzyme, or **lipase.**

The fats and oils are saponified by means of alkali on a very large scale, for the production of the ordinary **soaps.** When the fat is boiled with a solution of caustic soda it passes slowly into solution, for it is converted by the soda into a comparatively soluble sodium salt and the easily soluble glycerol. The equations for this reaction are as follows:—

$$(C_{15}H_{31}COO)_3C_3H_5 + 3NaOH = \underset{\text{Sodium palmitate}}{3C_{15}H_{31}.COONa} + C_3H_5(OH)_3$$

$$(C_{17}H_{35}COO)_3C_3H_5 + 3NaOH = \underset{\text{Sodium stearate}}{3C_{17}H_{35}.COONa} + C_3H_5(OH)_3$$

$$(C_{17}H_{33}COO)_3C_3H_5 + 3NaOH = \underset{\text{Sodium oleate}}{3C_{17}H_{33}.COONa} + C_3H_5(OH)_3$$

The solution thus obtained is a crude soap solution, which may be purified in various ways. For example, when strong brine is added to it, the sodium salts of the acids of the fats or oils are thrown out of solution by the presence of the sodium chloride. This process of "salting out," as it is termed, depends partly on the reduction in solubility of a salt when another salt containing a common ion (here sodium) is added to the solution, partly also because the soap exists to a certain extent in a state of colloidal solution and is thrown out by the addition of an electrolyte. The soap thus salted out may be separated, washed free from salt and glycerol, which remain in solution, and then melted up with a small proportion of water. When the mass cools it solidifies to a soap of the ordinary waxy consistency. The nature of the soap varies according to the character of the fat or oil taken, and to the degree of purification. **Castile soap** is made by the saponification of olive oil, and contains comparatively little stearate.

When potash is used instead of soda, the soap obtained is not as a rule purified, but is used as a gelatinous mass under the name of **soft soap.** The potassium salts of the fatty acids are considerably more soluble in water than the sodium salts. The pharmacopœial soft soap, or green soap, is prepared from olive oil. It dissolves readily in alcohol.

A lead soap is used as an adhesive under the name of **lead**

plaster. It may be prepared either by warming up olive oil and lead monoxide in presence of water, or by precipitation of an ordinary soap solution in warm water by means of a solution of lead acetate.

That a soap solution contains some substance not in true solution, but as a colloid, is evident from the fact that the concentrated soap solution made with warm water sets on cooling to a jelly. The true nature of soap solutions has not as yet been fully ascertained. They are always slightly alkaline by hydrolysis, since they are derived from a strong base and very feeble acids. They exhibit curious surface tension phenomena, and they readily emulsify, and detach in the form of fine particles, the greasy materials by means of which dust, etc., adheres to the skin or clothing; hence their use as cleansing agents.

The acids of the fats and oils are themselves insoluble, and so likewise are their salts, except those of the alkalies. If, therefore, a soap solution is acidified, an immediate precipitate of the acids is obtained. Similarly, if a calcium or magnesium salt is added to a soap solution, a precipitate of calcium or magnesium stearate, etc., is formed. It is on this account that hard waters, which contain calcium or magnesium salts in solution, use up a considerable quantity of soap before a lather is produced. If the water is very hard, the calcium and magnesium salts may be seen to separate out as a curdy precipitate.

Stearic acid is made on a considerable scale from fats, for use in the manufacture of candles. The hydrolysis of the fat is conducted either by means of superheated steam alone, or with the addition of a few per cent. of calcium hydroxide. The quantity of calcium hydroxide added is not sufficient to convert the whole of the ester into calcium salt; it apparently acts chiefly by accelerating the action of the steam. The calcium salt produced is converted into acid by the addition of the requisite quantity of sulphuric acid. Candles of which stearic acid is a constituent are generally known as "stearin" candles; they do not, however, contain stearin (*i.e.* tristearin) itself, but the corresponding acid.

When fats or oils become rancid, the chemical process which occurs is the hydrolysis of the esters into acids and

glycerol. The hydrolysis is here no doubt due to the action of the enzyme lipase, which often occurs associated with fats and oils. In recent years fats have been hydrolysed on a large scale for industrial purposes by means of a lipase, which may be readily obtained from castor-oil seeds.

Besides these ordinary animal fats and oils, several other high-boiling esters occur in nature. Thus, for example, **spermaceti**, a crystalline waxy substance which is found in the head of the sperm whale, seems to be an ester which consists mainly of cetyl palmitate. On hydrolysis this substance is decomposed into cetyl alcohol and palmitic acid, according to the equation—

$$\underset{\text{Cetyl palmitate}}{C_{15}H_{31}.COOC_{16}H_{33}} + H_2O = \underset{\text{Cetyl alcohol}}{C_{16}H_{33}OH} + \underset{\text{Palmitic acid}}{C_{15}H_{31}.COOH.}$$

Beeswax consists mainly of myricyl palmitate, with the formula $C_{15}H_{31}.COOC_{30}H_{61}$.

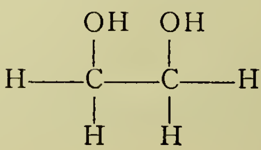
Lanoline is prepared from wool grease (which is exuded in the perspiration of sheep) by washing out all substances soluble in water, and contains among other things esters of acids with the alcohol isocholesterol, which has the empirical formula $C_{27}H_{45}OH$. Lanoline may be readily incorporated with about its own weight of water, and forms the basis of numerous ointments. Ordinary soft lanoline contains about 30 per cent. of water.

An isomeric alcohol, **cholesterol**, occurs in most animal tissues in conjunction with the fats. It forms a large proportion of the dry matter of the brain and nerves, and also of gall-stones.

POLYHYDRIC ALCOHOLS.

Glycol, $C_2H_4(OH)_2$.

Glycol is a dihydric alcohol derived from ethane, and possesses the formula—



To distinguish it from other substances of similar nature it is often called ethylene glycol, since it contains the group C_2H_4 of ethylene, and may be prepared from this substance as follows:—Ethylene unites directly with bromine in order to form ethylene bromide, $C_2H_4Br_2$. If this bromide is hydrolysed by means of water or a feebly alkaline solution — for example, a solution of potassium carbonate—it is converted into ethylene glycol—

$$C_2H_4Br_2 + K_2CO_3 + H_2O = C_2H_4(OH)_2 + 2KBr + CO_2.$$

Glycol is a thick, viscid liquid with a sweet and at the same time slightly burning or acrid taste. It boils at about 200°, and mixes in all proportions with water and alcohol. As the large proportion of hydroxyl in the molecule might lead us to expect, it is only sparingly soluble in ether, and scarcely at all in hydrocarbon solvents.

It may be seen from the graphic formula that ethylene glycol is doubly a primary alcohol, because it contains two groups, CH_2OH. In conformity with this constitution each of the carbons may be oxidised to the aldehyde group, $CO \cdot H$, and the acid group, COOH. When both primary alcohol groups are converted into carboxyl groups, the product is oxalic acid. Glycol, being a dihydric alcohol, can react with two molecules of monobasic acids. Thus when heated with hydrochloric acid to a high temperature it yields ethylene dichloride, according to the equation—

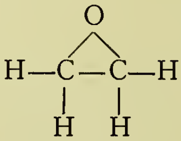
$$C_2H_4(OH)_2 + 2HCl = C_2H_4Cl_2 + 2H_2O.$$

At about 100° the action of gaseous hydrochloric acid on glycol does not go so far, an intermediate product named **ethylene chlorhydrin**, $C_2H_4(OH)Cl$, being produced—

$$C_2H_4(OH)_2 + HCl = C_2H_4(OH)Cl + H_2O.$$

When ethylene chlorhydrin is acted on by caustic alkali hydrochlorine acid is removed, and a substance named **ethylene oxide**, (C_2H_4O), is produced. This substance, which is a liquid of very low boiling-point (about 30°), is isomeric with acetaldehyde. It exhibits, however, none of the properties of an aldehyde, and receives the following formula, in which the oxygen atom

is not attached to a single carbon atom, as in an aldehyde, but is shared between two:—



Ethylene oxide

It unites readily with hydrochloric acid to regenerate ethylene chlorhydrin—

$$C_2H_4O + HCl = C_2H_4(OH)Cl.$$

Glycerol, $C_3H_5(OH)_3$.

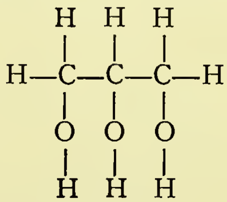
The trihydric alcohol glycerol is, as we have seen, produced by the hydrolysis or saponification of the fixed fats and oils. It is now largely prepared from the aqueous liquid from which soap has been separated. It is contained in solution along with large quantities of impurities, and the practical problem of the manufacture of glycerol is to separate it from these impurities. There are various methods by which this separation is effected. For example, the spent soap lyes may be treated with a mixture of ferrous and ferric sulphates. These substances react with the soap remaining in solution, and also with the excess of alkali used in the saponification. A precipitate of iron hydroxides and iron soaps is thus formed, and carries down with it all the other insoluble and colloidal substances. This precipitate is filtered off, and the liquor is concentrated by evaporation in a partial vacuum, the heating being done by means of steam-pipes immersed in the liquid. The reason why here, and in other similar cases, the concentration of the solution is effected in a vacuum is, that the water can be removed at a lower temperature in a partial vacuum than it can under atmospheric pressure, and thus decomposition by over-heating is avoided. The salts which were in solution crystallise out during this process of evaporation, and are suitably removed. When the liquor contains about 80 per cent. of glycerine it is distilled in as high a vacuum as possible by means of superheated steam. The distillate is finally concentrated to the requisite degree in vacuum pans.

Glycerol, like glycol, is a syrupy, viscid liquid with a sweetish taste. When perfectly pure it is a solid which melts at about 17°. It is, however, strongly hygroscopic, and always contains in ordinary circumstances small quantities of water which keep it liquid. It has the specific gravity of 1·26, mixes in all proportions with water and alcohol, but is practically insoluble in ether, chloroform, hydrocarbon solvents, and fixed oils. It is a useful solvent for many substances, and is largely used in medicine chiefly in conjunction with other drugs. When perfectly pure it boils without decomposition at 290°, but in the impure state it decomposes slightly at this temperature. One mode of decomposition which occurs when it is heated is represented by the following equation :—

$$C_3H_5(OH)_3 = \underset{\text{Acrolein}}{C_2H_3.CO.H} + 2H_2O.$$

The unsaturated aldehyde acrolein is easily recognised by its pungent, unpleasant smell, resembling that of formaldehyde, and its production can be conveniently used as a test for glycerol. As the decomposition takes place much more readily in presence of sulphuric acid or potassium hydrogen sulphate, these substances may be added to the glycerol before it is heated.

The following constitutional formula for glycerol—



Glycerol

shows that it contains two primary alcohol groups and one secondary alcohol group. In accordance with this it may be oxidised either to an aldehyde and acid on the one hand, or to a ketone on the other. The actual oxidation, however, is extremely difficult to regulate, so that the theoretical oxidation products of glycerol are usually obtained by other methods.

The action of hydrochloric acid on glycerol leads to the production of two isomeric monochlorhydrins of the formula

$C_3H_5Cl(OH)_2$, according as the hydroxyl group, which is replaced by chlorine, is on the middle or one of the external carbon atoms of the chain. The further action of hydrochloric acid yields dichlorhydrins of the formula $C_3H_5Cl_2(OH)$. When the dichlorhydrins are heated with phosphorus pentachloride the third hydroxyl group of the glycerol is replaced by chlorine, in accordance with the equation—

$$C_3H_5Cl_2(OH) + PCl_5 = \underset{\substack{\text{Trichlorhydrin of} \\ \text{glycerol} \\ \text{Trichloropropane}}}{C_3H_5Cl_3} + POCl_3 + HCl.$$

UNSATURATED OXIDISED COMPOUNDS.

ALLYL ALCOHOL, ACROLEIN, ACRYLIC ACID.

When glycerol is heated with crystallised oxalic acid, it loses water and is at the same time reduced by the oxalic acid, with formation of an unsaturated alcohol named allyl alcohol. The mechanism of the process is somewhat complicated, but the final result may be represented by the following equation:—

$$C_3H_5(OH)_3 + (COOH)_2 = \underset{\text{Allyl alcohol}}{CH_2:CH.CH_2OH} + 2H_2O + 2CO_2.$$

Allyl alcohol, $C_3H_5.OH$, is a liquid which boils at about 97°, and possesses a characteristic irritating odour. It has the properties both of an unsaturated compound and of a primary alcohol. Thus, when brought into contact with chlorine it combines with it as follows:—

$$CH_2:CH.CH_2OH + Cl_2 = CH_2Cl.CHCl.CH_2OH,$$

producing one of the dichlorhydrins of glycerol. Similarly, with bromine it produces a dibromhydrin. On careful oxidation it is converted first into acrylic aldehyde or acrolein—

$$\underset{\text{Allyl alcohol}}{CH_2:CH.CH_2OH} + (O) = \underset{\text{Acrolein}}{CH_2:CH.CO.H} + H_2O,$$

which in its turn by further oxidation produces acrylic acid—

$$CH_2:CH.CO.H + (O) = CH_2:CH.COOH.$$

Acrolein, $CH_2:CH.CO.H$.—It has already been noted that acrolein is produced by the dehydration of glycerol—

$$C_3H_5(OH)_3 = CH_2:CH.CO.H + 2H_2O.$$

It is thus apparent that glycerol and acrolein are at the same stage of oxidation, since one can be derived from the other by the simple removal of water. Acrylic aldehyde is a liquid boiling at about 50°, and is well characterised by its unmistakable, pungent odour. It exhibits the reaction of aldehydes and also of unsaturated compounds, combining readily, for example, with bromine to form dibromopropionic aldehyde, $CH_2Br.CHBr.CO.H$.

Acrylic acid, $CH_2:CH.COOH$, in a similar way gives the reactions both of an acid and of an unsaturated substance. It has an odour resembling that of acetic acid, and mixes with water in all proportions.

The radical **allyl**, $CH_2:CH.CH_2$, which occurs in allyl alcohol is common to a considerable number of compounds. For example, allyl iodide, $CH_2:CH.CH_2I$, may be prepared from allyl alcohol (or more conveniently from glycerol) by the action of phosphorus iodide. It resembles ethyl iodide in its properties, but in addition exhibits the reactions of an unsaturated substance It has a marked odour of garlic, the oil of which contains sulphur derivatives of allyl. Allyl isothiocyanate, $CH_2:CH.CH_2.NCS$, occurs as a glucoside in black mustard seeds.

MONOBASIC HYDROXY ACIDS.

Glycollic Acid, $CH_2(OH).COOH$.

When chlorine acts upon acetic acid the first product is monochloracetic acid, $CH_2Cl.COOH$. If the potassium salt of this acid is boiled with water, the chlorinated portion is hydrolysed, with production of hydrochloric acid, the chlorine being replaced by the hydroxyl group, according to the equation—

$$\underset{\text{Chloracetic acid}}{CH_2Cl.COOH} + H_2O = HCl + \underset{\text{Glycollic acid}}{CH_2(OH).COOH}.$$

We thus obtain from the chloroacid a hydroxy acid which is, in

this case, termed hydroxyacetic acid or **glycollic acid.** This substance is at once an acid, owing to the presence of the COOH group, and a primary alcohol, on account of the presence of the CH_2OH group. The hydroxy acids in general are thus at once alcohols and acids, and exhibit many of the reactions of both classes of substances. Since glycollic acid is a primary alcohol it can be oxidised to the corresponding aldehyde, and this aldehyde further oxidised to the corresponding acid. We therefore obtain by oxidation of glycollic acid the following substances:—

$$\underset{\text{Glycollic acid}}{CH_2(OH).COOH} + (O) = \underset{\text{Glyoxalic acid}}{H.CO.COOH} + H_2O$$

$$\underset{\text{Glyoxalic acid}}{H.CO.COOH} + (O) = \underset{\text{Oxalic acid}}{HO.CO.COOH}$$

of which glyoxalic acid is both aldehyde and acid, and oxalic acid a double acid, or, as we say, a dibasic acid.

Glycollic acid is a crystalline substance which is readily soluble in water, in alcohol, and in ether. It is used in physiological chemistry as a test substance for proteins, and usually occurs in small quantity in glacial acetic acid, which, therefore, generally gives with proteins the requisite reaction.

If we now consider the possible monobasic hydroxy derivatives of propionic acid, $CH_3.CH_2.COOH$, we see that there may be two of them, namely—

I.	II.
$CH_2(OH).CH_2.COOH.$	$CH_3.CH(OH).COOH.$
β-Hydroxypropionic acid	α-Hydroxypropionic acid

the acid corresponding to formula II. is systematically called α-hydroxypropionic acid, the acid corresponding to formula I. β-hydroxypropionic acid. This method of naming hydroxy and other derivatives of the fatty acids is based on the following principle. The carbon atom attached to the carboxyl group is called the α carbon atom, the next one is called the β carbon atom; then comes the γ carbon atom, then the δ, and so on. Thus, in valeric acid the carbon atoms may be distinguished by writing the Greek letters in association with them as follows—

$$\underset{\delta}{CH_3}.\underset{\gamma}{CH_2}.\underset{\beta}{CH_2}.\underset{\alpha}{CH_2}.COOH.$$

Lactic Acid, $C_3H_6O_3$.

α-Hydroxypropionic acid is commonly known as lactic acid, so called because it is the chief acid formed when milk turns sour by fermentation. It is prepared by the lactic fermentation of the milk-sugar. When milk is exposed to the air it is certain after a time to receive from the air a small quantity of an organism containing the enzyme **lactase**, which acts upon the milk-sugar, or lactose, and converts it into lactic acid. The chemical equation representing the action of the enzyme is—

$$\underset{\text{Lactose (milk-sugar)}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Lactic acid}}{4C_3H_6O_3}.$$

The enzyme is capable of turning other sugars besides lactase into lactic acid, which is therefore generally prepared from cane-sugar. The solution of cane-sugar is mixed with a little sour milk containing the lactic acid organism. The fermentation comes to an end before all the sugar is converted into lactic acid unless the lactic acid is neutralised as it is produced. This is usually effected by adding chalk to the sugar solution. Calcium lactate is thus formed, and may be separated from the filtered solution by crystallisation. From this calcium salt the acid may be liberated by addition of sulphuric acid.

Lactic acid is a viscous liquid which mixes with water, alcohol, and ether in all proportions. It cannot be purified by distillation, as it breaks up at its boiling-point into simpler products. Lactic acid in this respect resembles all hydroxy acids, which are decomposed on heating, sometimes only with elimination of water, sometimes with more profound changes.

A variety of lactic acid is found in muscle, and may be prepared from meat extract. It is named **sarcolactic acid**, and possesses the same constitutional formula as the lactic acid from carbohydrates.

Hydracrylic Acid, $CH_2(OH).CH_2.COOH$.

This acid, or β-hydroxypropionic acid, is not formed during lactic fermentation, but may be obtained by boiling β-chloropropionic acid with water, thus:—

$$CH_2Cl.CH_2.COOH + H_2O = CH_2(OH).CH_2.COOH + HCl.$$

It resembles lactic acid generally in its properties, but on heating breaks up into acrylic acid and water—

$$CH_2(OH).CH_2.COOH = CH_2:CH.COOH + H_2O.$$

This behaviour is characteristic of β-hydroxy acids, which similarly lose water on heating, with formation of $\alpha\beta$-unsaturated acids.

β-Hydroxybutyric acid, $CH_3.CH(OH).CH_2.COOH$.

This acid occurs in diabetic urine, and is a reduction product of acetyl-acetic acid (p. 126). Its relationship to acetyl-acetic acid is that of a secondary alcohol to the corresponding ketone, and its formation by reduction of acetyl-acetic acid may be represented by the following equation—

$$CH_3.CO.CH_2.COOH + 2(H) = CH_3.CH(OH).CH_2.COOH.$$

When heated it loses water, and gives rise to the unsaturated crotonic acid—

$$\underset{\beta\text{-Hydroxybutyric acid}}{CH_3.CH(OH).CH_2.COOH} = \underset{\text{Crotonic acid}}{CH_3.CH:CH.COOH} + H_2O.$$

γ- and δ-Hydroxy Acids—Lactones.

γ-Hydroxybutyric acid, $HO.CH_2.CH_2.CH_2.COOH$, is an example of γ-hydroxy acids. This substance even at the ordinary temperature loses water, but not in the same way as the β-hydroxy acids. The water is here eliminated, not between the alcoholic group and the neighbouring unoxidised carbon, but between the alcoholic group and the acid group, thus—

$$HO.CH_2.CH_2.CH_2.COOH = \underset{\text{Butyro-lactone}}{\overbrace{CH_2.CH_2.CH_2.CO}^{O}} + H_2O$$

The substance so produced is called a **γ-lactone**, and may be regarded as a kind of internal ester, the alcoholic and acid groups belonging to the same molecule. When treated with alkali, lactones are saponified and converted into the alkaline salt of the alcohol acid, *e.g.*—

$$\overbrace{CH_2.CH_2.CH_2.CO}^{O} + NaOH = HO.CH_2.CH_2.CH_2.COONa$$

δ-Hydroxy acids behave in the above respect like γ-hydroxy acids, giving rise spontaneously to δ-lactones, *e.g.*—

$$HO.CH_2.CH_2.CH_2.CH_2.COOH$$
δ-Hydroxyvaleric acid

$$= \overbrace{CH_2.CH_2.CH_2.CH_2.CO}^{O} + H_2O$$
Valero-lactone

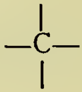
STEREOISOMERISM.

Sarcolactic acid, like fermentation lactic acid, is α-hydroxy-propionic acid. In all its chemical actions it behaves exactly like the lactic acid from milk, but differs from it in its effect upon polarised light. We are therefore confronted with the difficulty that we have only one formula to give to two different acids; for although lactic acid and sarcolactic acid are absolutely similar in their chemical properties, yet they differ in their physical properties in such a way that they cannot be regarded as identical substances. The mode of formulation, therefore, which we have so far adopted must be looked upon as erroneous, or at least imperfect. If we consider what our graphic formulæ directly represent to us, we find that they only state which atoms are directly united to each other, and say nothing about how these are actually arranged in the molecule. Thus the formulæ—

$$\begin{array}{c} H \\ | \\ Cl—C—Cl \\ | \\ H \end{array} \qquad\qquad \begin{array}{c} Cl \\ | \\ H—C—Cl \\ | \\ H \end{array}$$

are regarded as identical, for although they are different in appearance, yet they make exactly the same statement as to which atoms are directly united to each other. Suppose, however, we desire to look more closely into the structure of the molecules, and to consider not only the directness of union of the constituent atoms, but also their relative position in the molecule. It is evident that our formulæ give us no information as to this, for the simple reason that they represent on paper all the atoms as lying in one plane, or two dimensions, whereas in the molecule they must be conceived as being

arranged in space of three dimensions. Let us now, therefore, represent the carbon atom with its four valencies, not as formerly by the plane formula—



but by the solid formula—

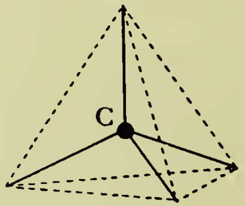


FIG. 15.

the four dark lines which represent the valencies of the carbon atom being regularly arranged in space, *i.e.*, directed towards the four solid angles of a regular tetrahedron, a three-sided pyramid, shown in dotted outline, of which each side and the base is an equilateral triangle. We may now write the space-formula of dichloromethane as follows, the tetrahedra alone being shown :—

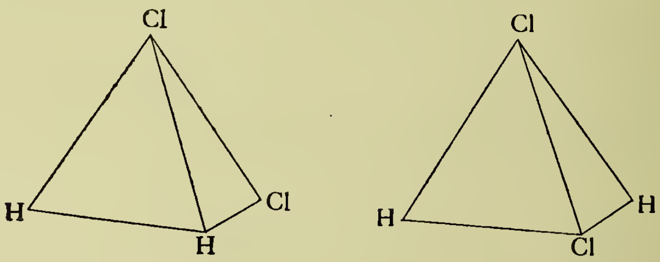


FIG. 16.

These formulæ on paper are apparently different, but if we consider the actual solids we find that they are the same, as the second formula may be made into the first by merely turning the solid through an angle of 120°. We say that here the two solids are superposable, meaning thereby that rotation of one solid as a whole will make it identical with the other. In this case, then, the space formulation yields nothing more

than the plane formulæ when taken to represent the mere directness of union of the atoms.

Consider now the formula of glycollic acid from this point of view, writing not the whole formula in space, but merely that of the carbon atom, which does not belong to the carboxyl group. We may, if we look down on the top of the pyramid and omit the central C representing this carbon atom, write, for example, the following varieties of the formula $CH_2OH \,.\, COOH$—

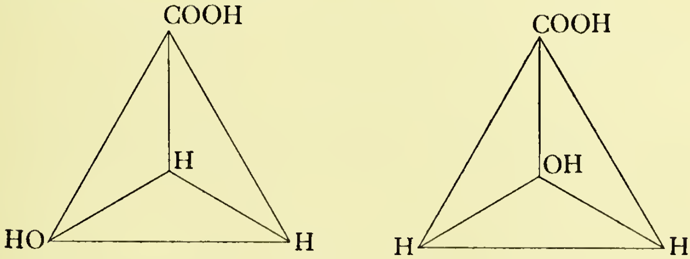


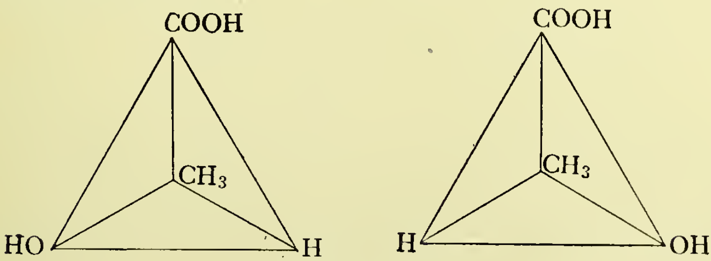
FIG. 17.

The lines here do not represent the directions of the valencies, but the edges of the pyramid as seen projected on the plane of the paper. A little consideration will show that these formulæ are superposable, *e.g.* identical, for by a simple rotation of the solid figure each can be converted into the other. The space-formulæ, then, lead in this case to nothing new.

Turn now to the space-formula of α-hydroxypropionic acid—

$$\begin{array}{c} CH_3 \\ | \\ H—C—COOH \\ | \\ OH \end{array}$$

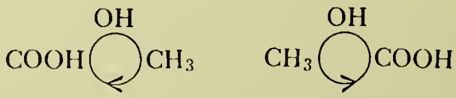
We may write this—



I. FIG. 18. II.

with other variations which are superposable on one or other of these. Careful consideration will show that formulæ I. and II. are not superposable on each other. No kind of rotation can make one fit over the other so that each group of the one falls over the corresponding group of the other. The formulæ differ from each other as a right hand differs from a left, and the formulæ can as little be made to fit as a right-hand glove can be made to fit a left hand. Each formula is the image of the other in a mirror, just as a right hand is the mirror image of a left hand, and the object and its mirror-image are here not superposable.

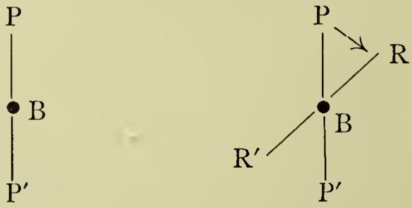
If we consider the arrangement of the groups OH, CH_3, and COOH in the order named, the hydrogen atom being now supposed at the apex of the pyramid, we see that in I. the order is clockwise, whilst in II. the order is opposite to this direction, thus :—



I. II.

This peculiarity of the space-formulæ is in accordance with the action of the lactic acids on polarised light.

In a ray of **polarised light**, as in a ray of ordinary light, the ether vibrates at right angles to the path of the ray; but whereas in ordinary light the vibrations take place in *all* directions at right angles to the ray, in polarised light the vibrations take place in *one* plane only. We consequently speak of the plane of polarisation of polarised light. Let the point B represent the path of a ray of polarised light looked at end



on, and coming towards the reader: then the line PP′ may represent the plane of polarisation of the ray, also looked at end on. If the ray is now made to pass through a solution of the lactic acid derived from muscle, it is found that the plane of polarisation has shifted to a new position, say RR′. A

similar solution of glycollic acid has no such effect. Lactic acid is therefore said to be **optically active**, and glycollic acid to be optically inactive.

The instrument by means of which the rotation is observed and measured is named a **polarimeter**, the structure of which is shown diagrammatically in Fig. 19. The apparatus consists essentially of two parts, the polarising part P, and the analysing part A, which can be rotated with respect to each other round their common axis. Between these may be placed a tube, T, containing the liquid, the rotation of which is to be determined. The ray of light from the source at L is made parallel by passing through a lens. It then reaches the Nicol's prism P which polarises it, after which it passes through a thin quartz plate, Q, extending only over a portion of the field, usually half. Quartz is an optically active solid which rotates the plane of polarisation of a ray of polarised light. In the absence of the tube T the ray, which now consists of two portions, one of which

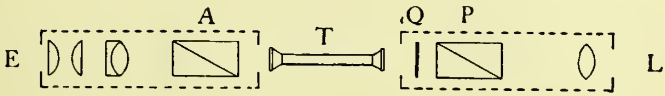


FIG. 19.

has passed through Q and the other not, reaches a second Nicol's prism, A, on emerging from which it passes through a series of telescopic lenses, focussed on Q, to the eye at E. The Nicol's prism P only allows light to pass through it which has vibrations in one definite plane, say the vertical plane. If in absence of the quartz plate and an optically active substance in the tube, the light reaches the second Nicol's prism, then if this second prism is placed similarly to the first, the light which is passed through the first prism will also pass through the second. If, however, the second prism is crossed with regard to the first, that is, turned through 90° from the parallel position, it stops all the light which has passed through the first, and the field appears dark.

If the quartz plate is now interposed between the prisms, and reaches only across half the field, the polarised light which is passed through it has the plane of its vibrations rotated slightly from the vertical, and so the portion of the field due to it will now appear illuminated, although the Nicols are crossed.

If the analysing Nicol is turned so that this half of the field shall appear dark, then the other half becomes illuminated. There is a position midway between these two points at which both halves of the field are feebly but equally illuminated. The appearance of the field in the three positions mentioned is shown in Fig. 20. The instrument is carefully adjusted to the position of equal illumination, and the angle indicated on the graduated circle attached to the analysing portion is read off. This is taken as the zero reading of the instrument, no optically active substance other than the quartz plate being present. If now an optically active substance is placed between the Nicols in the tube T, it rotates the plane of polarisation of both halves of the ray of light, and the field now appears unequally illuminated. The analysing portion is then turned until a position of equal illumination of the two halves of the field is again found. The position on the circle is again carefully read off, and the difference between this reading and the previous zero reading

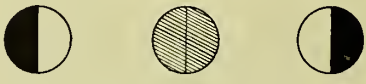


FIG. 20.

gives the angle through which the optically active substance has rotated the plane of polarisation of the ray.

The actual angle through which the plane is rotated depends on various circumstances, chiefly the concentration of the solution, the length of the layer of the liquid through which the polarised ray passes, and the specific rotatory power[1] of the substance. When the optically active substance in the above instance rotates the plane of polarisation in the direction of the clock, it is called dextro-rotatory (dextro-gyrate); when it rotates the plane of polarisation in the opposite sense, it is called lævo-rotatory (lævo-gyrate).

We have seen that there are two possible space-formulæ for a substance having the structural formula of lactic acid, and

[1] The specific rotatory power of a pure liquid is the rotation given by a column of the liquid 10 cm. long, divided by the density of the liquid. The wave-length of the monochromatic light employed must be specified. Thus the specific rotatory power of dextrolactic acid for the D line of sodium is given as $[\alpha]_D = +3\cdot5$. The + sign indicates that the substance is dextro-rotatory.

that one of these is in a sense dextro-gyrate whilst the other is lævo-gyrate. If these space-formulæ, therefore, are in accordance with fact, we might reasonably expect that to the dextro-rotatory sarcolactic acid there should correspond a lævo-rotatory isomeride which should rotate under similar conditions exactly as much to the left as sarcolactic acid rotates to the right, and this isomeride might conceivably be the ordinary lactic acid of fermentation. But by means of the polarimeter we find the latter to be optically inactive. Here there is apparent contradiction between the space-formulæ on the one hand, which predict two oppositely active lactic acids, and the actual isomerides, one of which is active and the other inactive. There is, however, a further possibility, namely, the existence of a mixture of the two oppositely active acids in equal proportions, which would be inactive, and might correspond to fermentation lactic acid. That this is in reality the case is proved by the possibility of splitting up fermentation lactic acid into two active acids, one of which is identical with sarcolactic acid, and the other different from it only in this, that it is lævo-rotatory to the same extent as sarcolactic acid is dextro-rotatory. If we employ the letters *d*- and *l*- to indicate dextro- and lævo-rotatory respectively, we see that there may be three α-hydropropionic acids, namely :—

d-lactic acid = Sarcolactic acid,
l-lactic acid = Lævolactic acid.
dl-lactic acid = Fermentation lactic acid,

the last named being inactive owing to the compensation of the *d*- and *l*- acids of which it consists. This compensation is indicated by the symbol *dl*, or sometimes by the letter *r*, which stands for *racemic*, a name frequently applied to inactive mixtures of active substances.

The space-formulæ, then, which we have adopted, *i.e.* those based on the conception of a so-called "tetrahedral" carbon atom, are in conformity with fact. This agreement holds good not only in the case of the lactic acids, but quite generally. Wherever we find an **asymmetric carbon atom**, *i.e.*, a carbon atom united to form different atoms or groups of atoms, the possibility of optical isomerism exists. Further instances of this type of isomerism will be found in the sequel. { for

KETO ACIDS.

Acetyl-acetic Acid, $CH_3.CO.CH_2.COOH$.

When ethyl acetate is warmed with metallic sodium, a vigorous reaction takes place and hydrogen is evolved, sodium being converted into sodium compounds which separate in the solid state. If the product is acidified in order to decompose these sodium compounds, it is found that a new ester has been produced, the equation representing its formation being as follows :—

$$\underset{\text{Ethyl acetate}}{CH_3.CO.OEt} + \underset{\text{Ethyl acetate}}{CH_3.CO.OEt} = \underset{\text{Ethyl acetyl-acetate}}{CH_3.CO.CH_2.COOEt} + \underset{\text{Ethyl alcohol}}{EtOH}.$$

This ester is the ethyl ester of acetyl-acetic acid, and is of great importance in synthetical chemistry. It will be observed that its formula contains the grouping $CO.CH_2.CO$. Wherever such a grouping occurs in the formula of a compound it is found that one or both of the hydrogens of the CH_2 group are capable of being replaced by a metal. This property would at first sight indicate that the substances containing this group were acid in character. They are not, however, acids in the ordinary sense, but may be compared rather with substances like alcohol, or with acetylene, rather than with acids proper, being only capable of forming metallic derivatives which can scarcely be regarded as salts.

Acetyl-acetic ester being a compound of this class, is capable of reacting with metallic sodium, or with an alcoholic solution of sodium ethoxide, to produce a sodium compound. The formation of this compound with sodium ethoxide may be represented as follows :[1]—

$$CH_3.CO.CH_2.CO.OEt + NaOEt$$
$$= CH_3.CO.CHNa.CO.OEt + EtOH.$$

[1] The abbreviated symbols Me, Et, Pr are frequently used instead of the formulæ CH_3, C_2H_5, C_3H_7, for methyl, ethyl, and propyl respectively, in order to economise space or to differentiate between two nodes of occurrence of the same radical.

It is owing to the possibility of forming such sodium compounds that acetyl-acetic ester and similar substances are of value in synthetical chemistry. For example, if we warm the sodium compound of acetyl-acetic ester with ethyl iodide, a double decomposition takes place, sodium iodide being produced, and the ethyl radical taking the place of the sodium atom. The equation representing this reaction may be written as follows:—

$$CH_3.CO.CHNa.CO.OEt + C_2H_5I$$
$$= CH_3.CO.CH(C_2H_5).CO.OEt + NaI.$$

Here a synthesis, or fresh carbon to carbon union, has been effected, and a more complicated carbon chain built up from simpler chains. Instead of ethyl iodide, practically any similar halogen compound may be used, so that the production of a great variety of different substances from acetyl-acetic ester is possible.

Acetyl-acetic ester itself and the synthetic derivatives from it are not of special importance, but they may often be transformed into other substances which are of importance either on account of their inherent properties, or on account of the light which they throw upon the constitution of other substances.

When acetyl-acetic ester, or any of its derivatives, is saponified at the ordinary temperature by means of alkali, the alkaline salt is produced thus—

$$CH_3.CO.CH_2.CO.OEt + KOH$$
$$= \underset{\gamma}{CH_3}.\underset{\beta}{CO}.\underset{\alpha}{CH_2}.CO.OK + EtOH.$$

If this salt is carefully acidified, acetyl-acetic acid is liberated and may be extracted from the solution with ether.

Acetyl-acetic acid is an example of the class of substances termed keto acids, because it contains both the characteristic acid group and the characteristic ketone group. It is in especial what we term a β-keto acid, the keto group being in the β position with reference to the carboxyl group. Such β-keto acids are unstable, all of them being decomposed on heating, and many of them decomposing even at the ordinary temperature. The decomposition of acetyl-acetic acid takes place with production of acetone and carbon dioxide, according to the equation—

$$CH_3.CO.CH_2.CO.OH = CH_3.CO.CH_3 + CO_2.$$

The ethyl-acetyl-acetic acid, the synthetic formation of whose ester was referred to above, decomposes similarly with production of carbon dioxide and ethyl-acetone or methyl-propyl-ketone—

$$CH_3.CO.CH(C_2H_5).CO.OH = \underset{\text{Methyl-propyl-ketone}}{CH_3.CO.CH_2.C_2H_5} + CO_2.$$

We thus see how it is possible to synthetise ketones by means of acetyl-acetic ester.

It is also possible to synthetise monobasic acids by means of the same substances. If, for example, the ethyl derivative of acetyl-acetic ester is saponified by boiling with concentrated alcohol potash, the potassium salt, which may be looked upon as the first product of the action of the potash, decomposes with excess of potassium hydroxide, and gives rise to potassium acetate and potassium normal butyrate, according to the equation—

$$\begin{aligned} CH_3.CO.CH(C_2H_5).CO.OK &+ KOH \\ &= CH_3.CO.OK + \underset{\text{Potassium butyrate}}{C_2H_5.CH_2.CO.OK} \end{aligned}$$

When the ethyl ester of acetyl-acetic acid is similarly treated, it yields potassium acetate alone—

$$CH_3.CO.CH_2.CO.OK + KOH = CH_3.CO.OK + CH_3.CO.OK.$$

Acetyl-acetic acid and its ester, even in dilute aqueous solution, assume a claret colour on addition of ferric chloride. This coloration with ferric chloride is useful as a test for acetyl-acetic acid in diabetic urine, in which it occurs in small quantities. A further test is to warm with dilute acid or alkali so as to effect the decomposition with production of acetone, which may then be tested for by the iodoform test.

DIBASIC ACIDS.

The most important dibasic organic acids are: oxalic acid, malonic acid, succinic acid, glutaric acid, and their derivatives. The formulæ of these acids are given below—

$\begin{array}{l} COOH \\ \vert \\ COOH \end{array}$	$\begin{array}{l} COOH \\ \cdot \\ CH_2 \\ \cdot \\ COOH \end{array}$	$\begin{array}{l} CH_2—COOH \\ \vert \\ CH_2—COOH \end{array}$	$\begin{array}{l} CH_2—COOH \\ \cdot \\ CH_2 \\ \cdot \\ CH_2—COOH \end{array}$
Oxalic acid	Malonic acid	Succinic acid	Glutaric acid

Each may be derived from its predecessor by the insertion of a CH_2 group in the carbon chain.

Oxalic Acid, $H_2C_2O_4$.

This dibasic acid occurs in many plants, chiefly in the form of the calcium salt, or of the acid potassium salt. Its sodium salt may be prepared by heating sodium formate to about 250°, the equation for the reaction being—

$$\underset{\text{Sodium formate}}{2H.COONa} = \underset{\text{Sodium oxalate}}{(COONa)_2} + H_2.$$

From this salt oxalic acid is liberated by the action of an equivalent quantity of a stronger acid such as sulphuric acid.

Oxalic acid crystallises from aqueous solution as a dihydrate, $H_2C_2O_4,2H_2O$, which on heating to 100° loses its water of crystallisation. The anhydrous acid sublimes at about 150°, and on being heated more strongly decomposes into water, carbon monoxide, and carbon dioxide, the same decomposition being readily effected by means of concentrated sulphuric acid.

Oxalic acid has somewhat feeble reducing properties, being oxidisable by oxidising agents to carbon dioxide and water—

$$H_2C_2O_4 + (O) = 2CO_2 + H_2O.$$

Thus, in hot acid solution it at once decolorises potassium permanganate.

Calcium oxalate, CaC_2O_4,H_2O, is one of the most characteristic salts of oxalic acid. It is very sparingly soluble in water, so that oxalates in solution are readily precipitated by solutions of calcium salts. It may be distinguished from the calcium salts of other organic acids by its insolubility in dilute acetic acid.

Oxalic acid is a much stronger acid than the simple monobasic acids like acetic acid, and acts, when taken internally, as an irritant poison. Neutral oxalates are much less poisonous, so that alkaline substances may be used as antidotes in oxalic acid poisoning, especially lime-water or chalk, which form with it the insoluble calcium salt.

Malonic Acid, $CH_2(COOH)_2$.

This acid is prepared by synthesis as follows:—Acetic acid is first converted by the action of chlorine into monochloracetic acid, which is then neutralised with potash, and the potassium salt boiled with a solution of potassium cyanide. Double decomposition takes place according to the following equation:—

$$\underset{\text{Potassium chloracetate}}{\begin{matrix} Cl \\ \cdot \\ CH_2 \\ \cdot \\ COOK \end{matrix}} + KCN = \underset{\text{Potassium cyanacetate}}{\begin{matrix} CN \\ \cdot \\ CH_2 \\ \cdot \\ COOK \end{matrix}} + KCl$$

When the potassium cyanacetate is heated with concentrated potash solution it is decomposed as follows:—

$$\underset{\text{Potassium cyanacetate}}{\begin{matrix} CN \\ \cdot \\ CH_2 \\ \cdot \\ COOK \end{matrix}} + KOH + H_2O = \underset{\text{Potassium malonate}}{\begin{matrix} COOK \\ \cdot \\ CH_2 \\ \cdot \\ COOK \end{matrix}} + NH_3$$

From the potassium salt malonic acid may be liberated by the addition of the requisite quantity of hydrochloric acid.

It will be observed that the synthesis proper—that is, the formation of a new carbon to carbon union—occurs during the double decomposition, in which the chlorine atom is replaced by the cyanogen radical CN. The malonic acid obtained in this way is still mixed with potassium chloride and ammonium chloride. The reaction product is filtered, and the solution evaporated to dryness. Since malonic acid is soluble in ether whilst the inorganic chlorides are insoluble, it may be extracted from the solid residue by means of this solvent, and afterwards purified by recrystallisation.

Malonic acid is a colourless crystalline solid which is easily soluble in water, alcohol, and ether. It melts at 132°, and at this temperature begins to decompose. At higher temperatures the decomposition is more rapid, the resulting products being acetic acid and carbonic anhydride, thus—

$$\underset{\text{Malonic acid}}{HOOC.CH_2.COOH} = \underset{\text{Acetic acid}}{CH_3.COOH} + CO_2.$$

This decomposition of malonic acid and its derivatives—that is, acids in which the hydrogen of the CH_2 group has been replaced by organic radicals—is a very important one, since it enables us to pass from derivatives of malonic acid, which are not in general themselves of importance, to derivatives of acetic acid, which are frequently important.

The ethyl ester of malonic acid, or **malonic ester**, as it is commonly called, may be obtained from the acid by warming it with ethyl alcohol and a little gaseous hydrogen chloride. It is not, however, necessary to prepare the acid itself in order to obtain the ester. If, after the double decomposition between the chloracetate and potassium cyanide, the solution is evaporated to dryness, then dissolved in ethyl alcohol and saturated with gaseous hydrogen chloride, malonic ester is obtained instead of malonic acid on addition of water. Malonic ester contains the group $CO.CH_2.CO$, the hydrogen of which is therefore capable, as in the case of acetyl-acetic ester, of being replaced, first by sodium through the action of sodium ethoxide, and then by alkyl radicals through double decomposition of the sodium compound with alkyl iodides. Thus diethyl-malonic ester may be prepared by the following series of reactions :—

$$\begin{array}{l} COOEt \\ \dot{C}H_2 \\ \dot{C}OOEt \end{array} + NaOEt = \begin{array}{l} COOEt \\ \dot{C}HNa \\ \dot{C}OOEt \end{array} + HOEt$$

$$\begin{array}{l} COOEt \\ \dot{C}HNa \\ \dot{C}OOEt \end{array} + C_2H_5I = \begin{array}{l} COOEt \\ \dot{C}H.C_2H_5 \\ \dot{C}OOEt \end{array} + NaI$$

$$\begin{array}{l} COOEt \\ \dot{C}H.C_2H_5 \\ \dot{C}OOEt \end{array} + NaOEt = \begin{array}{l} COOEt \\ \dot{C}Na.C_2H_5 \\ \dot{C}OOEt \end{array} + HOEt$$

$$\begin{array}{l} COOEt \\ \dot{C}Na.C_2H_5 \\ \dot{C}OOEt \end{array} + C_2H_5I = \begin{array}{l} COOEt \\ \dot{C}(C_2H_5)_2 \\ \dot{C}OOEt \end{array} + NaI$$

When the ester of diethyl-malonic acid is saponified by means of alcoholic potash, the corresponding potassium salt is formed, from which the acid may be derived by acidification, and subsequent extraction of the aqueous solution with ether. On heating, diethyl-malonic acid splits up in the same way as malonic acid, giving off carbon dioxide and leaving diethyl-acetic acid.

Succinic Acid, $C_2H_4(COOH)_2$.

Whilst this acid is not of the same importance in synthetic chemistry as malonic acid, its derivatives are of very considerable interest, both from a practical and theoretical point of view. Succinic acid itself occurs in nature chiefly in the substance amber, as its name indicates. It is also formed in small quantities as a by-product in the alcoholic fermentation of sugars. It is generally prepared by the distillation of amber. When the oily distillate is concentrated by evaporation, it partially solidifies on cooling to a mass of impure succinic acid, which is afterwards purified by recrystallisation. Succinic acid is a solid which melts at 185° and boils at 235°, partly unchanged and partly with decomposition. The chief product of decomposition is succinic anhydride, formed in accordance with the equation—

$$\underset{\text{Succinic acid}}{\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array}} = \underset{\text{Succinic anhydride}}{\left.\begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\right\rangle O} + H_2O$$

The production of the anhydride by heating the acid gives a characteristic test for succinic acid, as the vapour of the anhydride when inhaled even in very small quantity induces an irresistible tendency to cough. The alkyl derivatives of succinic acid similarly lose water readily on heating, with production of an anhydride, thus—

$$\underset{\text{Ethyl-succinic acid}}{\begin{array}{r} C_2H_5.CH.COOH \\ | \quad\quad\quad\; \\ CH_2.COOH \end{array}} = \underset{\text{Ethyl-succinic anhydride}}{\left.\begin{array}{r} C_2H_5.CH.CO \\ | \quad\quad\; \\ CH_2.CO \end{array}\right\rangle O} + H_2O$$

They thus differ notably from malonic acid and its derivatives, which on heating lose, not water, but carbon dioxide.

Succinic acid dissolves freely in water, and forms both normal and acid salts. The normal salts, with the exception of those of the alkalies, are insoluble or sparingly soluble in water.

POLYBASIC HYDROXY ACIDS.

Malic Acid, $COOH.CH_2.CH(OH).COOH$.

This acid is monohydroxy-succinic acid, and its constitution may be represented by the graphic formula—

$$\begin{array}{l} \quad\;\; OH \\ \quad\;\;\; | \\ H—\mathbf{C}—COOH \\ \quad\;\;\; | \\ \quad\;\; CH_2—COOH \end{array}$$

Malic acid

It will be noted that it contains one asymmetric carbon atom, printed in thick type in the formula, and therefore exhibits the same kind of isomerism as lactic acid; that is, it exists in a dextro-rotatory form, a lævo-rotatory form, and an inactive mixture of the two.

The inactive variety, namely, *dl*-malic acid, may be prepared from succinic acid. When succinic acid is attacked by bromine, one of the four hydrogens of the hydrocarbon portion of the molecule is replaced by bromine, and monobromo-succinic acid is thus produced. When this acid is treated with silver hydroxide, the silver and bromine combine to form silver bromide, and the place of the bromine in bromo-succinic acid is taken by hydroxyl—

$$\begin{array}{l} CHBr.COOH \\ | \\ CH_2.COOH \end{array} + AgOH = \begin{array}{l} CH(OH).COOH \\ | \\ CH_2.COOH \end{array} + AgBr$$

The lævo-rotatory modification occurs in nature in a great many plants, especially in unripe fruits. Thus it is found in unripe apples, from which mode of occurrence its name is derived, and also in the unripe berries of the mountain ash, from which it is usually prepared. The juice of the rowan berries contains the acid in solution, and is neutralised by boiling with milk of lime. The sparingly soluble calcium salt separates, and from this the

acid may be obtained after purification. This, the ordinary or *l*-malic acid, is freely soluble in water, and gives rise both to acid and normal salts.

If we consider its formula, we see that it is an α-hydroxyl acid with reference to one of the carboxyl groups, and a β-hydroxy acid with reference to the other. Now β-hydroxy acids generally lose water on heating, with production of an unsaturated acid. Consequently we might expect malic acid on heating to lose water in one or other of two ways, or even in both. As a derivative of succinic acid it might lose water between the two carboxyl groups, and give rise to an anhydride; as a hydroxy acid it might lose water and give rise to an unsaturated acid. As a matter of fact, both of these reactions may take place, and according to the conditions of heating, we may obtain from malic acid either an unsaturated acid, fumaric acid, or the anhydride of maleic acid, which is isomeric with fumaric acid. The formulæ of these substances are given below—

$$\begin{array}{l} CH.COOH \\ \parallel \\ CH.COOH \end{array} \qquad\qquad \begin{array}{l} CH—CO \\ \parallel \\ CH—CO \end{array}\!\!\!\!>O$$

Fumaric acid — Maleic anhydride

It should be noted that maleic acid and fumaric acid have the same structural formula, but the isomerism between them may be explained by writing space-formulæ for the acids by means of tetrahedral carbon atoms, although they contain no asymmetric carbon.

Tartaric Acid, $COOH.CH(OH).CH(OH).COOH$.

Tartaric acid is dihydroxy-succinic acid, and its structure is represented by the formula—

$$\begin{array}{c} H \\ | \\ HO—\mathbf{C}—COOH \\ | \\ HO—\mathbf{C}—COOH \\ | \\ H \end{array}$$

This formula, it will be observed, contains two asymmetric carbon atoms. It will further be noted that the two carbon

atoms are similar; that is, each asymmetric carbon atom is united to the same four groups, namely, H, OH, COOH, and CH(OH).COOH. Each of these carbon atoms has a certain action on polarised light which passes through the molecule, and as the two carbon atoms are similar the action of each on the polarised light will be of the same magnitude. If we, therefore, try to predict the action of the whole molecule on polarised light so as to obtain the theoretical number of optical isomers, we must take into account that each of the asymmetric carbon atoms may be dextro-rotatory or lævo-rotatory. We may then have in the molecule the combination of two dextro-rotatory carbon atoms, two lævo-rotatory carbon atoms, or, finally, one dextro-rotatory and one lævo-rotatory.

The acid in which both carbon atoms are dextro-rotatory is the optical opposite of that in which both carbon atoms are lævo-rotatory; that is, in solutions of equivalent concentration the angle of rotation exhibited by one acid is exactly equal and opposite to that exhibited by the other. When the two acids are mixed in solution in equal proportions, the resulting solution is optically inactive. So far, then, the phenomena exhibited exactly correspond to those shown by the lactic acids; we have a dextro-rotatory acid, a lævo-rotatory acid, and an inactive mixture of the two, in equal proportions. There is, however, in the case of tartaric acid an additional optically inactive modification—that, namely, in which one and the same molecule contains a dextro-rotatory and a lævo-rotatory carbon atom. This acid, which is inactive by *internal* compensation, is called **mesotartaric acid**, and is quite distinct in its properties from the inactive **racemic acid**, which is inactive by *external* compensation; the words internal and external being here applied to the molecule. The molecule of mesotartaric acid is inactive in itself; in the case of racemic acid we have an inactive mixture of active molecules, and the compensation is thus external to the molecule.

The possible isomers are thus—

Active .	*d*-tartaric acid	=	Ordinary tartaric acid
	l-tartaric acid	=	Lævotartaric acid.
Inactive	*dl*-tartaric acid	=	Racemic acid
	i-tartaric acid	=	Mesotartaric acid

The letter *i*- indicates the fundamental inactivity by internal compensation.

Dextrotartaric Acid.—This acid is the common tartaric acid of commerce. It is contained either as acid or as salt in the juice of a considerable number of fruits, and is especially abundant in the grape. When grape juice undergoes fermentation for the manufacture of wine, a deposit of potassium hydrogen tartrate is formed towards the end of the fermentation. This salt is only sparingly soluble in water, and still less soluble in water containing alcohol. Consequently, as alcohol accumulates during the fermentation, potassium hydrogen tartrate begins to separate as a crystalline precipitate. The crude salt is termed **argol**, and is usually highly coloured, especially if red grapes are used in the fermentation. It is purified first of all by recrystallisation, and is then generally converted into calcium tartrate, which is nearly insoluble in water. The conversion is effected by first of all treating the potassium hydrogen tartrate with calcium hydroxide or calcium carbonate. The action which takes place is as follows:—

$$2KHC_4H_4O_6 + Ca(OH)_2 = K_2C_4H_4O_6 + CaC_4H_4O_6 + 2H_2O.$$

The insoluble calcium tartrate is filtered off, and the solution of the normal potassium salt is now mixed with calcium chloride, which precipitates the rest of the tartaric acid as calcium salt, potassium chloride remaining in solution—

$$K_2C_4H_4O_6 + CaCl_2 = CaC_4H_4O_6 + 2KCl.$$

The calcium tartrate after washing is decomposed with the requisite quantity of sulphuric acid—

$$CaC_4H_4O_6 + H_2SO_4 = CaSO_4 + H_2C_4H_4O_6.$$

The solution of tartaric acid is now filtered from the insoluble calcium sulphate, and evaporated until crystallisation takes place.

Tartaric acid crystallises well, forming large transparent crystals, which dissolve readily in water and in alcohol, but not in ether. They melt with decomposition at about 165°. When tartaric acid is heated more strongly, an odour resembling that of burnt sugar is perceived.

Being a dibasic acid, potassium tartrate forms both normal and acid salts. Normal *potassium tartrate*, $K_2C_4H_4O_6$, is readily soluble in water, but the *acid potassium tartrate*, $KHC_4H_4O_6$, known when purified as **cream of tartar**, is only soluble to the extent of 0·5 per cent. The corresponding acid sodium salt is easily soluble, and is sometimes used as a test substance for potassium, since with moderately concentrated solutions of neutral potassium salts it gives a precipitate of potassium hydrogen tartrate. One of the commonest of the normal tartrates is the mixed salt $KNaC_4H_4O_6,4H_2O$, which is called **Rochelle salt** or Seignette salt. It is prepared by neutralising potassium hydrogen tartrate with sodium carbonate or hydroxide, and crystallising—

$$KHC_4H_4O_6 + NaOH = KNaC_4H_4O_6 + H_2O.$$

It crystallises well, and is thus easily purified.

Potassium antimonyl tartrate, or **tartar emetic**,

$$K(SbO)C_4H_4O_6,\tfrac{1}{2}H_2O,$$

is a common medicinal preparation of antimony, and is made by dissolving antimony trioxide in a hot solution of potassium hydrogen tartrate—

$$2KHC_4H_4O_6 + Sb_2O_3 = 2K(SbO)C_4H_4O_6 + H_2O.$$

Like other hydroxy acids, tartaric acid when mixed with excess of alkali has the power of retaining cupric compounds in alkaline solution. Such a solution made from copper sulphate, Rochelle salt, and caustic soda, is largely used in testing for reducing sugars, and is known as **Fehling's solution**.

Lævotartaric acid and its salts resemble the corresponding dextro compounds in every respect, except that they have an equal and opposite rotatory power, and in some instances exhibit slight differences in crystalline form.

Mesotartaric acid differs from either the dextro- or lævorotatory acid by crystallising with one molecule of water of crystallisation instead of separating out in the anhydrous state. Its acid potassium salt is easily soluble in water, and generally speaking its salts have different solubilities from those of the two preceding acids.

Racemic acid.—This inactive mixed acid sometimes occurs along with ordinary tartaric acid in grape juice. It can be obtained by mixing solutions of the dextro and lævo acids in equal proportions. If such a solution is evaporated, the dextro and lævo acids separate out together as mixed crystals, different from those of the single acids, the formula of which is $2C_4H_6O_6,2H_2O$. Corresponding to racemic acid are salts called racemates, which differ from the salts of the optically active tartaric acids in their solubility and in their crystalline form.

Citric Acid.

$$\begin{array}{l} CH_2.COOH \\ | \\ CH(OH).COOH \\ | \\ CH_2.COOH \end{array}$$

$CH_2 . COOH$
$C(OH) . COOH$
$CH_2 . COOH$

Citric acid resembles tartaric acid somewhat closely in its properties. Like tartaric acid it is a hydroxy acid, but is tribasic instead of dibasic. It will be noticed that the formula contains no asymmetric carbon atom, so that citric acid does not exhibit optical activity, and only occurs in one modification. The acid itself, mixed with a small proportion of its calcium salt, occurs in the juice of lemons, and is prepared from this juice industrially. It is also possible to obtain it from glucose by a process of fermentation. The purification of the citric acid as it exists in lemon juice is carried out in much the same way as the purification of tartaric acid. The citric acid is converted into its calcium salt, which is almost insoluble in hot water, by neutralising with lime, and this calcium salt is then decomposed by the requisite quantity of sulphuric acid.

Citric acid is extremely soluble in water, somewhat less soluble in alcohol, and only sparingly soluble in ether. It separates from moderately warm aqueous solution in large prismatic crystals, which contain one molecule of water of crystallisation. It loses this water of crystallisation a little above 100°, and melts at 153°. At a higher temperature it decomposes, giving off water and forming an unsaturated acid. When heated rapidly it chars like tartaric acid; but, unlike tartaric acid, it gives no smell of burnt sugar. Being a hydroxy

acid, it has the property of keeping copper dissolved in alkaline solution.

The neutral potassium salt $K_3C_6H_5O_7$ is used in medicine, and so likewise are a solution of the ammonium salt, a solution of the double salt of bismuth and ammonium, and ferric ammonium citrate.

ESTERS OF INORGANIC ACIDS.

We have seen that the compounds of the halogens with the alkyl radicals—for example, ethyl chloride—may be regarded as esters of the halogen acids. Indeed the name ethyl chloride in itself is sufficient to suggest this. If, instead of the halogen acids we consider such inorganic acids as nitrous acid, nitric acid, and sulphuric acid, we find that esters can be derived from them, and that these esters have properties closely analogous to those derived from organic acids. Many of them are of considerable importance in medicine and industrial chemistry.

Esters of Nitrous Acid.

Ethyl nitrite, $C_2H_5O\,.\,NO$.—This substance may be prepared by adding a mixture of alcohol, water, and sulphuric acid to a solution of an alkali nitrite, the mixture being kept cool during the process. The sulphuric acid liberates nitrous acid from the nitrite, which at once reacts with the alcohol, giving rise to ethyl nitrite—

$$2NaNO_2 + H_2SO_4 + 2C_2H_5OH = Na_2SO_4 + 2C_2H_5O.NO + 2H_2O.$$

The ethyl nitrite, if a sufficiency of water has been added, separates as an oily liquid, which can be collected, dried, and purified by distillation. It has a pleasant odour and is decomposed by the action of alkalies, with formation of an alkali nitrite and ethyl alcohol—

$$C_2H_5O\,.\,NO + NaOH = NaNO_2 + C_2H_5OH.$$

It is used in medicine in dilute alcoholic solution, and is also a constituent of "sweet spirit of nitre," formed by the action of nitric acid on alcohol and metallic copper.

Amyl nitrite, $C_5H_{11}O\,.\,NO$, is prepared in a similar way to

ethyl nitrite, amyl alcohol being used instead of ethyl alcohol. It is administered for medicinal purposes by inhalation of the vapour.

Esters of Nitric Acid.

Ethyl nitrate, $C_2H_5O.NO_2$.—If ordinary nitric acid is allowed to act upon ethyl alcohol, ethyl nitrate is produced, but at the same time oxidation of the alcohol by the nitric acid occurs. In this process of oxidation the nitric acid is reduced to nitrous acid, so that the principal product of the action of nitric acid on ethyl alcohol is ethyl nitrite rather than ethyl nitrate, some of the alcohol being oxidised to aldehyde. In order, therefore, to prepare ethyl nitrate from ethyl alcohol, it is necessary to add to the reacting mixture some substance which will destroy nitrous acid as soon as it is formed. Urea is a suitable substance for this purpose. It reacts at once with nitrous acid with elimination of nitrogen, thus—

$$\underset{\text{Urea}}{CO(NH_2)_2} + \underset{\text{Nitrous acid}}{2HO.NO} = CO_2 + 3H_2O + 2N_2,$$

so that although some of the alcohol is lost by oxidation, the only ester formed from it by nitric acid in presence of urea is ethyl nitrate. Ethyl nitrate is a volatile liquid with a pleasant odour. It is almost insoluble in water, and is readily hydrolysed by solutions of the alkalies with formation of an alkaline nitrate and ethyl alcohol.

Glyceryl trinitrate, *nitroglycerin*, $C_3H_5(O.NO_2)_3$.—This substance is prepared industrially on a very large scale. The name nitroglycerin, by which it is usually known, gives a wrong indication of its nature. It is not a nitro derivative, but an ester derived from nitric acid and the trihydric alcohol glycerol. It is prepared by slowly dropping glycerol into a well-cooled mixture of concentrated sulphuric acid and fuming nitric acid in the proportions of about four of the former and one of the latter. The chemical action which takes place is represented by the equation—

$$\underset{\text{Glycerol}}{C_3H_5(OH)_3} + 3HNO_3 = \underset{\text{Glycerol trinitrate}}{C_3H_5(O.NO_2)_3} + 3H_2O.$$

The function of the sulphuric acid is to moderate the reaction by dilution, and to bind the water which is formed as a product

of the reaction. After the reaction is complete the product is run into cold water. The nitroglycerin separates as a heavy oil, which is afterwards very thoroughly washed with cold water and left to dry in the air. Great care must be taken in the preparation and handling of nitroglycerin, as it is an excessively explosive substance, particularly when not quite pure.

That it is an ester can be shown by the action of alkalies. Thus, when saponified by means of caustic potash solution it yields, as chief products, glycerol and potassium nitrate—

$$C_3H_5(O.NO_2)_3 + 3KOH = 3KNO_3 + C_3H_5(OH)_3.$$

These are, however, not the only products of the action of alkali on nitroglycerin, as oxidation and reduction actions occur at the same time.

Nitroglycerin is a heavy colourless oil practically insoluble in water, freely soluble in alcohol and ether. It is without odour, and has a slightly sweetish and pungent taste. It is used in medicine for certain heart affections, but its chief use is in the manufacture of explosives. By itself it is too dangerous and explosive to handle. It may, however, be mixed with diatomaceous earth, or kieselguhr, which is a light absorbent powder consisting of the siliceous skeletons of minute marine organisms. This comparatively safe mixture, in which the diatomaceous earth plays no part chemically, is known by the name of **dynamite.** The explosive character of nitroglycerin is due to the circumstance that it contains both an oxidising and an oxidisable portion. Once chemical action has started between these two portions of the substance, it proceeds with excessive rapidity, giving instantaneously a comparatively great volume of gas at a high temperature and under high pressure, all the products of the reaction being gaseous. It is not only used as an explosive by itself, but also as an ingredient in many other explosive substances. **Cordite**, for example, is a gelatinous substance made by dissolving gun-cotton in nitroglycerin and forming the mixture into threads or cords before it has set.

Esters of Sulphuric Acid.

Generally speaking, when sulphuric acid acts on a monohydric alcohol it produces, not a dialkyl sulphate, but an alkyl

hydrogen sulphate. The same class of substance is formed when an alcohol is brought into contact with sulphuric anhydride. Thus, from ethyl alcohol we obtain ethyl hydrogen sulphate—

$$C_2H_5OH + H_2SO_4 = C_2H_5.HSO_4 + H_2O$$
$$C_2H_5OH + SO_3 = C_2H_5.HSO_4$$

Ethyl hydrogen sulphate, $SO_2\begin{cases} OH \\ OC_2H_5. \end{cases}$ This substance, having still one replaceable hydrogen of the sulphuric acid, behaves as an acid, and is known as **sulphovinic acid.** It is easily soluble in water, but cannot be crystallised from water, because on evaporation of its solution it is hydrolysed in accordance with the equation—

$$\underset{\text{Ethyl-hydrogen sulphate}}{HO.SO_2.OC_2H_5} + H_2O = \underset{\text{Sulphuric acid}}{HO.SO_2.OH} + C_2H_5OH.$$

It acts as a powerful monobasic acid, and may readily be distinguished from sulphuric acid by its barium salt, which, unlike barium sulphate, is freely soluble in water. It occurs to a small extent in urine, in which it may be tested for as follows:— The urine is acidified with hydrochloric acid, and to the solution barium chloride is added; the sulphates are immediately precipitated as barium sulphate. The solution is now filtered and the filtrate boiled with water, the action of which is accelerated by the presence of hydrochloric acid. The ethyl hydrogen sulphate is hydrolysed with formation of sulphuric acid, and a second precipitate of barium sulphate is obtained as the boiling proceeds.

When heated by itself or with concentrated sulphuric acid, ethyl hydrogen sulphate splits up into sulphuric acid and ethylene (p. 64)—

$$C_2H_5HSO_4 = H_2SO_4 + C_2H_4.$$

When heated with alcohol, it gives rise to sulphuric acid and ether (p. 69)—

$$C_2H_5HSO_4 + C_2H_5OH = (C_2H_5)_2O + H_2SO_4.$$

Methyl sulphate, $(CH_3)_2SO_4$.—When methyl alcohol and

sulphuric anhydride are brought together at a low temperature they combine, with formation of methyl hydrogen sulphate—

$$CH_3OH + SO_3 = CH_3 . HSO_4.$$

This substance when heated alone does not decompose in the same way as ethyl hydrogen sulphate, but splits up into dimethyl sulphate and sulphuric acid—

$$2CH_3 . HSO_4 = \underset{\text{Dimethyl sulphate}}{(CH_3)_2SO_4} + H_2SO_4.$$

Dimethyl sulphate is a heavy liquid which boils at about 190°, and the vapours of which are poisonous. It is used in organic chemistry as a methylating agent, owing to its great tendency to part with one of the methyl groups and take up hydrogen in its stead to form methyl hydrogen sulphate. Thus, all alcoholic substances react with it according to the following scheme:—

$$ROH + (CH_3)_2SO_4 = ROCH_3 + CH_3 . HSO_4.$$

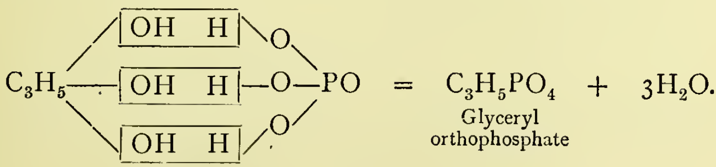
Esters of Phosphoric Acid.

Orthophosphoric acid, being a tribasic acid, is capable of forming three kinds of esters, *e.g.*—

$(C_2H_5)_3PO_4$	Triethyl phosphate
$(C_2H_5)_2HPO_4$	Diethyl hydrogen phosphate
$C_2H_5 . H_2PO_4$	Ethyl dihydrogen phosphate

Esters of the last two types are at the same time acids.

Glycerophosphoric acid is an important substance of the diacid class. Glycerol is a trihydric alcohol, orthophosphoric acid a tribasic acid. Thus they are theoretically capable of reacting molecule for molecule with elimination of three molecules of water—

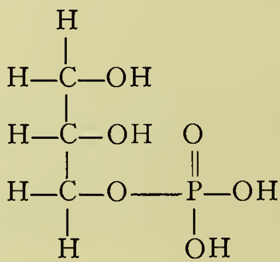


When glycerol and orthophosphoric acid are heated together,

however, the chief product is glycerophosphoric acid, only one molecule of water being eliminated—

$$C_3H_5(OH)_3 + H_3PO_4 = \underset{\text{Glycerophosphoric acid}}{C_3H_5(OH)_2.H_2PO_4} + H_2O.$$

This acid is of much physiological interest, as it is a product of decomposition of many important substances, *e.g.* lecithin. Its graphic formula is—



ORGANIC SULPHUR COMPOUNDS.

THIOALCOHOLS, THIOETHERS, AND THEIR OXIDATION PRODUCTS.

Corresponding to the alcohols and ethers, compounds exist which contain sulphur in the molecule instead of oxygen, *e.g.*—

C_2H_5OH	Ethyl alcohol	$(C_2H_5)_2O$	Ethyl ether
C_2H_5SH	Ethyl mercaptan	$(C_2H_5)_2S$	Ethyl sulphide

Ethyl mercaptan, *ethyl hydrogen sulphide*, $C_2H_5.SH$, may be prepared by heating potassium ethyl sulphate or ethyl chloride with potassium hydrogen sulphide—

$$KC_2H_5SO_4 + KSH = K_2SO_4 + C_2H_5SH$$
$$C_2H_5Cl + KSH = KCl + C_2H_5SH$$

It is a liquid of offensive odour which boils at 36°. Unlike alcohol, it is sparingly soluble in water, and oxidises on exposure to air to diethyl disulphide—

$$4C_2H_5SH + O_2 = 2(C_2H_5)_2S_2 + 2H_2O.$$

Nitric acid oxidises it to ethane-sulphonic acid (compare benzene-sulphonic acid, p. 179)—

$$C_2H_5SH + 3(O) = \underset{\text{Ethane-sulphonic acid}}{C_2H_5.SO_2.OH.}$$

The hydrogen of the SH group is readily replaceable by heavy metals, in particular by mercury; whence the name mercaptan (*mercurio aptum*).

Ethyl sulphide, $(C_2H_5)_2S$.—When ethyl potassium sulphate is heated with potassium sulphide, double decomposition occurs and ethyl sulphide distils off—

$$2C_2H_5KSO_4 + K_2S = 2K_2SO_4 + (C_2H_5)_2S.$$

It is a volatile liquid of disagreeable odour. When oxidised by nitric acid, it yields the following substances:—

$$\underset{\text{Diethyl sulphide}}{(C_2H_5)_2S} \longrightarrow \underset{\text{Diethyl sulphoxide}}{(C_2H_5)_2SO} \longrightarrow \underset{\text{Diethyl sulphone}}{(C_2H_5)_2SO_2}.$$

Diethyl sulphone, $C_2H_5 . SO_2 . C_2H_5$, is the sulphur analogue of a ketone, $C_2H_5 . CO . C_2H_5$, just as a sulphonic acid, $C_2H_5 . SO_2 . OH$, is the sulphur analogue of a carboxylic acid, $C_2H_5 . CO . OH$.

Sulphonal, $(CH_3)_2C(SO_2C_2H_5)_2$.—This substance is extensively used as a hypnotic, and is prepared as follows. Ethyl mercaptan in presence of hydrochloric acid reacts with acetone according to the following equation:—

$$\underset{\text{Acetone}}{\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CO} + \underset{\text{Ethyl mercaptan}}{\begin{matrix} HSC_2H_5 \\ HSC_2H_5 \end{matrix}} = \underset{\text{Acetone mercaptole}}{\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} SC_2H_5 \\ SC_2H_5 \end{matrix}} + H_2O.$$

The mercaptole, which is a sulphide, may be oxidised to the corresponding sulphone, sulphonal, by means of potassium permanganate—

$$\underset{\text{Acetone mercaptole}}{\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} SC_2H_5 \\ SC_2H_5 \end{matrix}} + 4(O) = \underset{\text{Sulphonal}}{\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} SO_2 . C_2H_5 \\ SO_2 . C_2H_5 \end{matrix}}$$

Sulphonal is a tasteless and inodorous substance, sparingly soluble in cold water. It melts at 125°.

Trional, $(CH_3)(C_2H_5)C(SO_2C_2H_5)_2$, is prepared in the same way as sulphonal; methyl ethyl ketone, $CH_3 . CO . C_2H_5$, instead of acetone is used as starting-point. It has similar properties, and melts at 75°.

Tetronal, $(C_2H_5)_2C(SO_2C_2H_5)_2$, which is also employed as a hypnotic, is prepared from diethyl ketone, $C_2H_5 . CO . C_2H_5$, and melts at 85°.

DISTILLATION OF COAL.

When coal is heated to a high temperature in absence of air, useful products are obtained in great variety. The chief of these is illuminating gas, or coal-gas, and it is generally for obtaining this product that the industry is carried on.

For the production of coal-gas, the coal is heated in long fireclay retorts to a temperature of 1000° or over. These retorts have an iron mouthpiece by means of which they are connected with pipes, the further ends of which dip for a few inches under the surface of water contained in a covered trough, called the hydraulic main. At the high temperature employed, the organic compounds contained in the coal are decomposed, and pass off for the most part as gases or vapours. A portion of the original coal remains behind in the retort as gas-coke, which is a porous and impure variety of carbon, containing as it does practically all the ash in the original coal. With regard to the portion of the decomposition products passing off in the form of gas or vapour, a distinction may be made in respect of their behaviour on being cooled in contact with water. Some of the vapours are condensed to the liquid form, the liquid remaining undissolved by the water; some of them dissolve in the water of the hydraulic main; and some which escape solution remain gaseous and pass on for further purification.

Dealing first of all with that portion of the gases which escapes the cooling and solvent action of the water in the hydraulic main, we have to note the purifying processes through which this gas must pass in order that it may be available for illuminating purposes. First it is passed through air-cooled or water-cooled pipes or condensers, in which it deposits tarry material, portions of which may still be carried over mechanically with it in the form of fine particles. It then passes through washers and scrubbers, in which it comes into very intimate contact with water in order that the last quantities of tar and

substances soluble in water may be removed. It finally passes through lime purifiers—that is, vessels filled with slaked lime—which remove from it acid gases such as carbon dioxide, carbon disulphide, and sulphuretted hydrogen. The purified gas is stored in gasometers over water, and delivered from these gasometers under slight pressure, for domestic and other purposes.

Coal-gas varies greatly in composition according to the quality of coal used and the temperature employed in its distillation. The following table gives the approximate composition of ordinary samples of coal-gas:—

Hydrogen	50
Methane	30
Carbon monoxide	10
Ethylene, etc.	3·5
Carbon dioxide	2
Oxygen	0·5
Nitrogen	4
	100

It will be observed that the principal constituents of the coal-gas, although combustible, burn with a non-luminous or feebly luminous flame. The illuminating power of the gas is chiefly due to unsaturated hydrocarbons, of which ethylene, acetylene, and benzene vapours are the chief. As the analysis shows, these unsaturated substances exist in very small proportions in the gas, yet their presence is indispensable if the gas is to be used directly as an illuminant. For heating purposes, or for burning mixed with air in a burner for incandescent lighting, the presence of these substances is not necessary. The oxygen, carbon dioxide, and nitrogen which the coal-gas contains may be regarded as impurities.

It has been said that the water in the hydraulic main dissolves out certain of the vapours which are produced in the distillation of the coal. These vapours are chiefly derived from ammonium salts; for example, ammonium carbonate and ammonium sulphide. The solution of these salts is known as the **ammoniacal liquor** of the gasworks, and from this liquor pure ammonium salts are prepared by liberating the ammonia from it by means of lime, and afterwards absorbing the gas in the appropriate acids.

Coal-tar.

Coal-tar is that portion of the products of distillation of coal which condenses in the hydraulic main and condensers without dissolving in water. It is a black, oily liquid, considerably heavier than water, and possesses a characteristic, unpleasant odour. The crude substance is used to some extent as a preservative for wood, and also as a protective coating for metal pipes, etc., but the bulk of it is subjected to a further process of distillation which separates it into fractions, from which many valuable substances may be obtained by further purification. The iron stills in which the distillation takes place are of large capacity, holding many tons of the crude tar, and are usually arranged so that internal heating by means of steam coils may be used as an auxiliary to the external heating by means of fuel. The distillation must at first be conducted very carefully, since frothing takes place owing to the expulsion of gases dissolved in the tar, and to gaseous products from the small quantity of ammoniacal liquor with which the crude tar is still associated. When these substances have been got rid of, the distillation proper begins, the vapours being condensed in a cooled receiver. The number of fractions that are collected varies considerably, but the following main products may be noted:—

Light oil, boiling below 170°.
Carbolic oil, between 170° and 230°.
Creosote oil, from 230° to 270°.
Anthracene oil, or Green oil, above 270°.

The residue in the still, when the distillation is stopped, consists of **pitch**, which is run out while still warm.

The **light oil** has mixed with it a certain quantity of aqueous distillate from which it may be separated mechanically; the name light oil indicates that it is a substance insoluble in water and lighter than water. It consists principally of the hydrocarbons benzene, toluene, and the xylenes, along with smaller quantities of acidic and basic substances and heavy oils. It is subjected to further fractionation into two portions, the lower boiling of which consists of the crude hydrocarbons, and is known as naphtha. The higher boiling portion is added to the creosote oil. The crude naphtha is agitated with a solution of caustic soda in order to remove acidic substances

as soluble sodium salts. After washing with water it is then treated with a small quantity of concentrated sulphuric acid, which dissolves out basic substances and other impurities. The acid is then thoroughly washed out from the hydrocarbons by means of water, and the hydrocarbons are separated by further fractional distillation, the extent to which the fractionation is carried depending upon the degree of purity required in the various substances. The boiling-points of the hydrocarbons concerned are given in the following table:—

		B. Pt.
Benzene		80·5°
Toluene	Toluene	110°
Orthoxylene		142°
Metaxylene	Xylol	139°
Paraxylene		138°

The **carbolic oil** contains chiefly carbolic acid (boiling-point, 183°) and naphthalene (boiling-point, 218°). The latter is a solid substance which partially crystallises out when the oil cools. The crystals may be removed, pressed free from oil, and further purified by treatment with sulphuric acid, washing, and distillation or sublimation. The oil from which the naphthalene crystals have separated is worked up for carbolic acid by a process which will be described later (p. 162).

Creosote oil may also be used as a source of naphthalene, but it is chiefly employed in the crude state as a preservative for timber.

From the **green oil**, anthracene (boiling-point, 350°) and other solid hydrocarbons separate on cooling, and may be further purified by pressing, washing, and distillation.

BENZENE AND ITS HOMOLOGUES.

Benzene, C_6H_6.

We have seen that benzene is the most volatile of the hydrocarbons derived from coal-tar. Its boiling-point is 80·5°, that is, about 30° lower than the boiling-point of toluene, which forms the next higher fraction. Notwithstanding this difference of boiling-point, it is not easy to free benzene from toluene by fractional distillation. The separation of the last traces of toluene and other hydrocarbons may be most easily carried out

by freezing the benzene, *i.e.*, by a process of fractional crystallisation. When cooled by means of ice, or, better, by a freezing mixture, benzene solidifies, whereas toluene and the other hydrocarbons remain liquid and may be removed from the crystallised benzene. The crystals of pure benzene melt at about 5°.

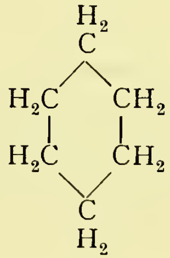
At the ordinary temperature benzene is a colourless liquid, of specific gravity 0·88, which possesses a characteristic smell resembling, when very dilute, that of coal-gas. It burns with a luminous smoky flame, and the small quantity of it contained in coal-gas is responsible for a great proportion both of the luminosity and the odour of the gas. Like other hydrocarbons, it is nearly insoluble in water. In the partially purified state it is extensively used as a solvent for fats, resins, etc. The molecular formula of benzene is derived from observations of its vapour density, and is C_6H_6. Benzene has thus the same percentage composition as acetylene, C_2H_2, and it may be derived in small quantity from acetylene by passing the latter through a red-hot tube. It differs from acetylene, however, in many important respects. Whereas acetylene is an active and highly unsaturated compound, benzene, on the other hand, is comparatively inactive, and resembles a saturated rather than an unsaturated compound, although it has points in common with both. It does not, for example, like acetylene, combine readily with bromine to form an addition compound. When bromine acts on benzene it does so by substitution rather than addition, according to the equation—

$$\underset{\text{Benzene}}{C_6H_6} + Br_2 = \underset{\text{Bromobenzene}}{C_6H_5Br} + HBr;$$

so that benzene here behaves like a saturated hydrocarbon. There must, therefore, be something in the constitution of benzene which makes it take a position apart from the unsaturated hydrocarbons proper, and endows it with properties resembling those of a saturated hydrocarbon.

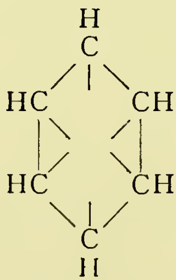
The saturated hydrocarbon containing six atoms of carbon is hexane, with the formula, C_6H_{14}. When benzene is treated with the most powerful hydrogenising agents, it takes up eight atoms of hydrogen, and is converted into normal hexane of the formula given above. Since the saturated hydrocarbon of benzene has no branch chain, it may be assumed that benzene itself has an unbranched chain. The first clue to its constitution

is found in the fact that when it is hydrogenised by the comparatively mild process of passing its vapour along with hydrogen over gently heated and finely divided metallic nickel, it yields a hydrocarbon of the composition C_6H_{12}, which acts entirely as a saturated hydrocarbon, and shows none of the reactions of unsaturated hydrocarbons whatever. Since this hydrocarbon C_6H_{12} is still two hydrogen atoms short of complete saturation, and yet contains no unsatisfied valencies or bonds, we are led to write its formula as follows :—



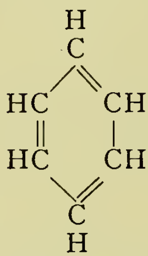
A hydrocarbon with such a formula is called a ring hydrocarbon, or a **cyclic** hydrocarbon, and that with which we are dealing receives the name of **cyclohexane**.

It is natural, then, in view of the fact that benzene may be easily hydrogenised to cyclohexane, to assume that it also has cyclic structure, and a consideration of its properties leads to the conclusion that in passing from cyclohexane to benzene one atom of hydrogen is removed from each atom of carbon in the cyclohexane. The formula of benzene is, therefore—

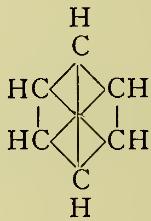


In this formula there are still six blank valencies, which no doubt in some way satisfy or saturate each other. We are, however, without definite knowledge as to how these valencies

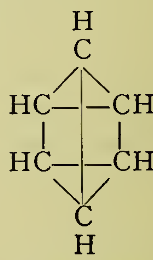
are arranged, and we are therefore unable to write a completely satisfactory formula of benzene. The following three formulæ have been proposed, but no one is wholly satisfactory :—



Kekulé's formula



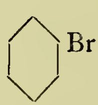
Centric formula



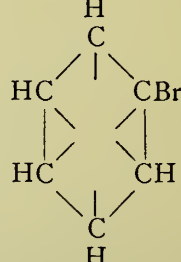
Prism formula

Kekulé's formula is that which is most frequently used, but in what follows we shall generally write the formula without indicating the position of the blank bonds, and indeed for the most part we shall make use of a further simplification and merely write a hexagon, thus—

to indicate the formula of benzene. At each angle of the hexagon there is supposed to be a carbon atom with its associated hydrogen atom. If we wish to indicate a derivative of benzene such as the bromobenzene, obtained by action of bromine on benzene, we merely write the substituting atom or radical at a corner of the hexagon, understanding thereby that the bromine or other group has taken the place of the hydrogen which was originally attached to the carbon at that angle. Thus the two formulæ—



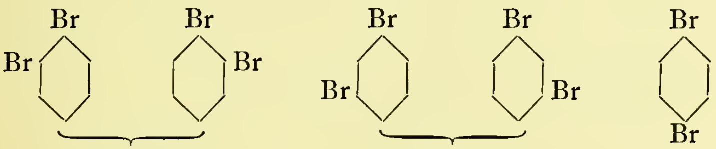
and



are on this understanding equivalent.

Since the constitutional formula of benzene is perfectly symmetrical, it is plainly a matter of indifference which of the six hydrogens we replace by another atom or group of atoms to obtain a mono-derivative of benzene. For a given substituting atom or radical, therefore, there is only one mono-derivative of benzene possible. Thus, there is only one monobromobenzene, one monomethyl-benzene, one mono-hydroxybenzene, etc. If, however, we introduce a second bromine atom into the benzene molecule in order to obtain a dibromobenzene, it is evident that more than one isomer is possible. The isomerism here is caused by the position of the bromine atoms relatively to each other. If we fix the position of one bromine atom, say, at the top of the hexagon, then a second bromine atom may be introduced at any other of the five angles of the hexagon, and we obtain the following formulæ:—

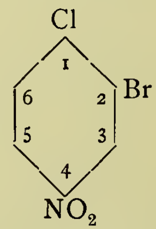
I. II. III. IV. V.



ortho *o*- meta *m*- para *p*-

Comparing these formulæ with each other, we see that I. is identical with II., for in both of these formulæ the bromine atoms are on neighbouring carbon atoms. Similarly, III. is identical with IV., one carbon atom intervening between the two to which the bromines are attached. Formula V. is different from any of the others, two carbon atoms coming between those which are attached to bromine. Our method of formulating benzene, therefore, predicts the existence of three different di-derivatives of benzene, in this instance of three di-bromobenzenes. The formula is satisfactory in this respect, because three isomeric di-substitution products of benzene actually exist, and no more than three. In order to distinguish between these three varieties by name, we use the prefixes *ortho*, *meta*, and *para*. The ortho di-derivatives are those corresponding to formulæ I. and II., in which the substituting radicals are on neighbouring carbon atoms; the meta derivatives correspond to formulæ III. and IV., and the para derivatives to formula V.

For more complex derivatives it is customary to number the angles of the hexagon, or the carbon atoms if we write the formula in full. The numbers may be started from any particular carbon atom, and are always read successively, going round the hexagon in the direction of the hands of a watch. Thus the name of the substance having the following constitution formula :—

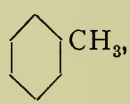


would be 1-chlor-2-brom-4-nitrobenzene.

It will be noted that here the chlorine and bromine atoms are in the ortho position, the chlorine atom and the nitro group in the para position, and the bromine atom and nitro group in the meta position, with regard to each other.

The Methyl Derivatives of Benzene.

According to the scheme of isomerism given above there is only one monomethyl-benzene. This substance has the formula

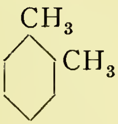


or still more briefly, $C_6H_5 . CH_3$. The radical C_6H_5, derived from benzene by the loss of one hydrogen atom, is called **phenyl.** The methyl derivative of benzene is therefore composed of two radicals, phenyl and methyl, united together. It may be regarded not only as methyl-benzene, but also as phenyl-methane. It is customary to regard all substances containing the benzene nucleus as derivatives of benzene, and classify them together as **aromatic** substances. We thus say that benzene is the simplest aromatic hydrocarbon, and it is convenient to distinguish in this way between the aromatic substances, or derivatives of benzene and similar cyclic compounds, on the one hand, and on the other those substances with

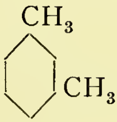
which we have been hitherto concerned, which are frequently grouped together as **fatty** or **aliphatic** substances, because the fats belong to this latter class. Though the classification is convenient, it must, of course, not be taken literally. Many "aromatic" substances have no odour, or one which is the reverse of aromatic in the ordinary sense; whilst many "fatty" substances have no connection whatever with the natural fats.

It has already been stated that methyl-benzene or **toluene** occurs in the hydrocarbons distilled from coal-tar. It can also be prepared by the dry distillation of balsam of Tolu, whence its name is derived. It is like benzene in appearance, but differs in its odour. It boils at 110°, and cannot be frozen by means of an ordinary freezing mixture.

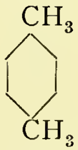
Commercial **xylene** contains the three isomeric substances



Orthoxylene or *o*-Xylene



Metaxylene or *m*-Xylene



Paraxylene or *p*-Xylene

Xylol

in varying proportion, along with other hydrocarbons in smaller quantity.

Benzene, toluene, and the xylenes have all an antiseptic and preservative action on organic matter, even the small quantity dissolved in water having a noticeable effect. Mixtures of these three hydrocarbons, in various proportions according to the method of fractionation adopted, are extensively used as solvents. In particular, a mixture of toluene and the xylenes known as solvent naphtha is employed commercially as a solvent for rubber.

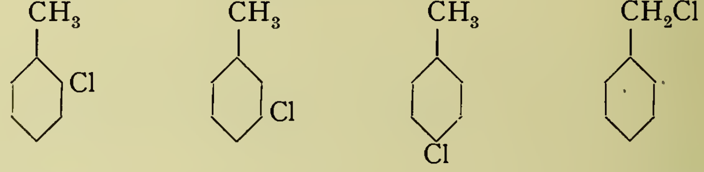
AROMATIC HALOGEN DERIVATIVES.

The halogen derivatives of benzene differ considerably in their properties from the halogen derivatives of fatty hydrocarbons. They are in particular more stable, inasmuch as the halogen atom attached to a carbon atom of the benzene nucleus is not easily removed or replaced by another radical. An

alcoholic solution of ethyl bromide, for example, gives, when warmed with an alcoholic solution of silver nitrate, an immediate precipitate of silver bromide, which slowly increases in quantity. On the other hand, an alcoholic solution of phenyl bromide or bromobenzene, C_6H_5Br, may be warmed with the alcoholic solution of silver nitrate for a very long time before any precipitate of silver bromide is apparent. Again, whilst the alkyl bromides are readily hydrolysed by alkalies, the aromatic bromo-compounds, such as bromobenzene, can with difficulty be hydrolysed at all.

If we consider the substituting action of chlorine on a hydrocarbon such as toluene, we see that it may take place in two distinct ways. Either the chlorine atom may replace a hydrogen atom belonging to the benzene ring, or it may replace a hydrogen atom of the fatty group CH_3. Either of these reactions may occur according to the conditions selected for the chlorination. If chlorine is passed into boiling toluene in bright sunlight, it replaces hydrogen of the methyl group, and not of the phenyl group. If, on the other hand, chlorine is passed into cold toluene in presence of a small quantity of iodine, or of iron, it displaces hydrogen of the phenyl group almost exclusively. The iodine or iron in such cases is said to act as a halogen carrier, playing the part of a catalyst and facilitating the introduction of the halogen.

The action of chlorine on toluene might therefore lead to the four following monochloro-derivatives:—



o-Chlorotoluene *m*-Chlorotoluene *p*-Chlorotoluene Benzyl chloride

The substances in which hydrogen of the aromatic nucleus is replaced by chlorine are called chlorotoluenes: the substance in which the hydrogen of the fatty side chain is replaced by chlorine is, to distinguish it from the others, called benzyl chloride. Corresponding to the difference in position of the chlorine atom, the chlorotoluenes differ very considerably in

their properties from the isomeric benzyl chloride. In the former the chlorine is attached to a carbon of the aromatic nucleus, and is therefore difficult to displace, whereas in the latter it is attached to the fatty portion of the molecule, so that is comparatively easily displaced. Thus, if benzyl chloride is boiled for a long time with water, hydrolysis occurs, according to the following equation :—

$$\underset{\text{Benzyl chloride}}{C_6H_5.CH_2Cl} + H_2O = \underset{\text{Benzyl alcohol}}{C_6H_5.CH_2OH} + HCl.$$

whilst the chlorotoluenes are quite unaffected by this treatment.

According to the ordinary system of deriving the names of radicals from hydrocarbons, the univalent radical C_6H_5 derived from benzene should be called benzyl. Before this systematic nomenclature had been adopted, however, the name **benzyl** was given to the radical $C_6H_5.CH_2.$ derived from toluene. The name is still retained for this radical, the radical C_6H_5 receiving the name phenyl. The name **tolyl**, derived in the customary way from toluene, is applied to those radicals of the formula $CH_3.C_6H_4.$ which have been formed from toluene by removal of a hydrogen atom from the aromatic nucleus, and which are therefore isomeric with benzyl, where the hydrogen has been removed from the fatty side chain.

AROMATIC ALCOHOLS, ALDEHYDES AND ACIDS.

We have seen that when benzyl chloride is hydrolysed by water it yields benzyl alcohol, $C_6H_5.CH_2.OH$. This is an alcohol which behaves in general like the fatty alcohols. Thus it is readily acted upon by sodium, according to the following equation :—

$$\underset{\text{Benzyl alcohol}}{2C_6H_5.CH_2.OH} + 2Na = \underset{\text{Sodium benzoxide}}{2C_6H_5.CH_2.ONa} + H_2,$$

and by the action of phosphorus pentachloride is reconverted into benzyl chloride—

$$C_6H_5.CH_2.OH + PCl_5 = C_6H_5.CH_2Cl + HCl + POCl_3.$$

Since it contains the group CH_2OH, benzyl alcohol is a primary alcohol, and capable of oxidation to an aldehyde and

to an acid, the relationship of the three substances being shown by the following formulæ:—

$C_6H_5.CH_2OH$	Benzyl alcohol
$C_6H_5.CO.H$	Benzaldehyde
$C_6H_5.COOH$	Benzoic acid

Benzaldehyde, $C_6H_5.CO.H$.

This is a typical aromatic aldehyde. It was formerly called **oil of bitter almonds**, because it was obtained by the hydrolysis of the glucoside amygdalin (p. 211), which occurs in bitter almonds. It may be conveniently prepared by the simultaneous hydrolysis and oxidation of benzyl chloride. To effect these reactions the benzyl chloride is boiled with a solution of copper nitrate in a flask provided with a reflux condenser. The copper nitrate is partially hydrolysed by the water, with production of a small quantity of nitric acid. At the same time the benzyl chloride is hydrolysed, with production of benzyl alcohol and hydrochloric acid. The nitric acid then acts on the benzyl alcohol and oxidises it to benzaldehyde. Once the action is begun, the hydrochloric acid liberated by the hydrolysis of the benzyl chloride reacts upon the copper nitrate, with production of nitric acid, and the oxidising action thus goes on more briskly. These reactions may be represented by the following equations:—

$$Cu(NO_3)_2 + 2H_2O \rightleftharpoons Cu(OH)_2 + 2HNO_3$$
$$C_6H_5.CH_2Cl + H_2O = C_6H_5.CH_2OH + HCl$$
$$Cu(NO_3)_2 + 2HCl \rightleftharpoons CuCl_2 + 2HNO_3$$
$$2C_6H_5.CH_2OH + 2HNO_3 = 2C_6H_5.CO.H + 3H_2O + N_2O_3$$

The benzaldehyde formed may be extracted by means of ether, and purified by converting it into the sodium bisulphite compound (p. 74), from which it is regenerated by means of sulphuric acid.

Benzaldehyde is a colourless, highly refracting liquid, slightly heavier than water, in which it is only sparingly soluble. It boils at 180°, and has a pleasant aromatic odour. It is chiefly used in the manufacture of dyes, but also to some extent for flavouring.

Benzaldehyde resembles the fatty aldehydes in most of its

properties, but there are some important points of difference. For example, although it oxidises slowly in air at the ordinary temperature to form benzoic acid, yet it does not reduce Fehling's solution. Again, although it combines readily, like the fatty aldehydes, with sodium bisulphite and with hydrocyanic acid, it does not combine with ammonia to form an aldehyde ammonia. Instead of forming the usual addition compound with ammonia it reacts with it, with elimination of water, a complex substance named hydrobenzamide being formed—

$$3C_6H_5.CO.H + 2NH_3 = 3H_2O + \underset{\text{Hydrobenzamide}}{(C_6H_5.CH)_3N_2}.$$

The action of caustic potash on benzaldehyde also differs from its action on the fatty aldehydes. When shaken with a concentrated solution of caustic potash, benzaldehyde is partly reduced to benzyl alcohol and partly oxidised to benzoic acid, which is then neutralised with formation of potassium benzoate—

$$\underset{\text{Benzaldehyde}}{2C_6H_5.CO.H} + KOH = \underset{\text{Benzyl alcohol}}{C_6H_5.CH_2.OH} + \underset{\text{Potassium benzoate}}{C_6H_5.COOK}.$$

Benzaldehyde does not polymerise like the fatty aldehydes, and does not undergo the aldol condensation. When warmed, however, with an alcoholic solution of potassium cyanide, it does condense, but in a different manner, forming a substance named benzoin—

$$\underset{\text{Benzaldehyde}}{C_6H_5.CO.H + H.CO.C_6H_5} = \underset{\text{Benzoin}}{C_6H_5.CO.CH(OH).C_6H_5}.$$

It will be noted that benzoin contains the group CO.CH(OH), which group we have seen to exist in the sugars and give them their reducing action. Benzoin, in accordance with this, reduces Fehling's solution, although the aldehyde of which it is the condensation product does not.

Like the fatty aldehydes, benzaldehyde reacts with hydroxylamine and phenylhydrazine to form an oxime and a hydrazone respectively.

Benzoic Acid, $C_6H_5.COOH$.

This acid is slowly formed from benzaldehyde by atmospheric oxidation. It occurs as free acid in gum-benzoin

and other resins, and the substance hippuric acid, which is contained in considerable quantities in the urine of horses and other ruminants, yields benzoic acid on hydrolysis with acidulated water. Benzoic acid may be manufactured by the oxidation of benzyl chloride with moderately concentrated nitric acid—

$$C_6H_5.CH_2Cl + 2HNO_3 = C_6H_5.COOH + HCl + H_2O + N_2O_3.$$

Benzoic acid occurs as soft lustrous crystals, which are very sparingly soluble in cold water, but easily soluble in boiling water and in most organic solvents. It may be purified readily by sublimation. The odour of its vapour is of a pleasant aromatic character, but when inhaled it provokes irritation in the throat and induces coughing. Most of the salts of benzoic acid are soluble in water; the ferric salt, however, is thrown out as a buff-coloured precipitate when a solution of ferric chloride is added to a soluble benzoate.

Benzoic acid and several of its salts are used in medicine. The acid itself has antiseptic properties, and is sometimes employed as a preservative.

There are not the same points of difference between aromatic and fatty carboxylic acids as there are between aromatic and fatty aldehydes. Generally speaking, the reactions of benzoic acid with various reagents are the same as those exhibited by the fatty acids. Thus, phosphorus pentachloride acts on benzoic acid to produce benzoyl chloride—

$$C_6H_5.COOH + PCl_5 = \underset{\text{Benzoyl chloride}}{C_6H_5.CO.Cl} + HCl + POCl_3.$$

This acyl chloride, **benzoyl chloride**, $C_6H_5.CO.Cl$, must be clearly distinguished from the alkyl chloride, benzyl chloride, $C_6H_5.CH_2.Cl$. Whilst the latter is only decomposed by prolonged boiling with water, the former is decomposed by water, like other acyl chlorides, at the ordinary temperature—

$$C_6H_5.CO.Cl + H_2O = C_6H_5.COOH + HCl.$$

The anhydride, **benzoic anhydride**, $(C_6H_5.CO)_2O$, may be formed by warming together benzoyl chloride and sodium benzoate—

$$C_6H_5.CO.Cl + C_6H_5.COONa = NaCl + (C_6H_5.CO)_2O.$$

The **esters** of benzoic acid are readily produced by boiling the acid with the corresponding alcohol and a little mineral acid, *e.g.*—

$$C_6H_5.COOH + C_2H_5OH = \underset{\text{Ethyl benzoate}}{C_6H_5.COOC_2H_5} + H_2O.$$

Ethyl benzoate formed in this way is an oil possessing a pleasant aromatic smell, and may be readily saponified by boiling with a solution of alcoholic potash—

$$C_6H_5.COOC_2H_5 + KOH = C_6H_5.COOK + C_2H_5OH.$$

PHENOLS

Besides the aromatic alcohols such as benzyl alcohol, another class of aromatic hydroxy compounds exists—that, namely, of the phenols. In the aromatic alcohols the hydroxyl group is attached to a carbon atom which is not a member of the benzene ring. In the phenols, on the other hand, the hydroxyl group is attached directly to a carbon of the aromatic nucleus. This difference in constitution is connected with a great difference in properties. Whereas the aromatic alcohols are neutral substances, the phenols are distinctly acid in character, some of the replaced phenols being as strongly acid as the powerful mineral acids. Several of these phenols are found in coal-tar, and from this substance phenol itself is prepared.

Phenol, $C_6H_5 . OH$.

On account of its acid properties phenol is also known by the name of **carbolic acid.** It occurs in considerable quantity along with other phenols in the fraction of the coal-tar distillate known as carbolic oil. When the naphthalene has been crystallised out from this fraction (p. 149), the oil remaining may be treated with dilute caustic soda which, forming a soluble sodium salt with phenol, dissolves it out and leaves the neutral and basic substances unaffected. When the aqueous solution is concentrated and made acid with sulphuric acid, the crude phenol separates as an oil, which on cooling crystallises partially to solid phenol.

Pure phenol is a colourless crystalline solid which melts at 42°. On exposure to light in presence of air, the phenol assumes a pink colour. It is sparingly soluble in cold water, but the addition of a small quantity of water to the solid phenol liquefies it. Thus, if crystallised phenol is shaken up in its own weight

of water, two liquid layers will form, the upper layer being water with about 7 per cent. of phenol dissolved in it, the lower layer being phenol with about 7 per cent. of water dissolved in it. Although it is only sparingly soluble in water, it dissolves very readily in alkaline solutions, owing to its acidic character. When, therefore, the crystals are shaken up with caustic soda solution they dissolve at once, with formation of *sodium phenoxide* (also called sodium phenolate or sodium carbolate):—

$$C_6H_5OH + NaOH = C_6H_5ONa + H_2O.$$

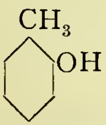
Phenol can be readily recognised by its characteristic odour. It is a powerful germicide, and solutions of it are frequently employed for antiseptic purposes. It is also an important raw material in the manufacture of many drugs, dyes, and explosives.

Solutions of phenol give a violet coloration with ferric chloride. This test is given not only by phenol itself, but by a great many other substances containing phenolic hydroxyl groups, that is, hydroxyl attached directly to a carbon of the aromatic nucleus. The presence of the hydroxyl group makes it much easier to replace some of the hydrogen atoms still remaining by other atoms or radicals. Thus, for example, if bromine water is added to a solution of phenol, an immediate precipitate of tribromophenol is produced—

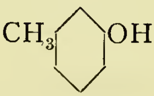
$$C_6H_5.OH + 3Br_2 = C_6H_2Br_3.OH + 3HBr.$$

Bromine water under similar conditions would have practically no action on benzene itself or any of the benzene hydrocarbons.

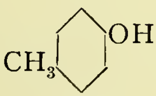
Homologues of Phenol.—Several homologues of phenol occur along with phenol itself in coal-tar, but the pure substances are not generally prepared from this source. Three monomethyl-phenols exist. These are known as **cresols**, and crude cresol is a mixture of the three isomers, the formulæ of which are—



o-Cresol



m-Cresol



p-Cresol

These substances all melt at a lower temperature than phenol, and the mixture of them is at the ordinary temperature a liquid. What is known as "commercial carbolic acid" contains little phenol, and consists chiefly of a mixture of the cresols.

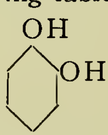
The cresols, like phenol, have a powerful antiseptic action, and the crude substances are much used as constituents of antiseptic mixtures. These mixtures are frequently made by emulsifying the phenols with a soap. For example, crude carbolic acid may be boiled up with palm oil, soda ash, and water. The resulting product on dilution with water easily forms an emulsion which acts as a powerful antiseptic.

Thymol, 1 : 3 : 6-$C_6H_3(OH)(CH_3).CH(CH_3)_2$.—This methyl-isopropyl-phenol is found in oil of thyme, from which it may be prepared in the crystalline state. It melts at 44°, and has a pleasant odour of thyme. It has marked antiseptic properties, and is used in medicine both externally and internally.

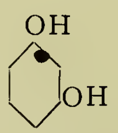
Dihydric Phenols.

Just as it is possible to obtain dihydric and trihydric alcohols, such as glycol, $C_2H_4(OH)_2$, and glycerol, $C_3H_5(OH)_3$, so it is possible to obtain from benzene not only phenol itself, but dihydric and trihydric derivatives, which retain the characteristic properties of a phenol.

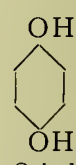
The formulæ of the three dihydroxy-benzenes are given in the following table :—



Catechol
(Pyrocatechin)



Resorcinol
(Resorcin)



Quinol
(Hydroquinone)

Catechol, *orthodihydroxy-benzene,* 1 : 2-$C_6H_4(OH)_2$, is most conveniently prepared from a natural substance which is its methyl ether. This substance occurs in beechwood tar, and is named **guaiacol.** The methyl group of guaiacol is replaced by hydrogen when the substance is heated with a concentrated solution of hydriodic acid—

$$\underset{\text{Guaiacol}}{C_6H_4(OH)(OCH_3)} + HI = \underset{\text{Catechol}}{C_6H_4(OH)_2} + CH_3I.$$

Catechol is also obtained by the dry distillation of catechu. It is a colourless solid which melts somewhat above the boiling-point of water. Having two hydroxyl groups in the molecule, it is much more soluble in water than phenol, and its aqueous solution gives a green coloration on an addition of ferric chloride. If sodium bicarbonate solution is added to the green liquid, the colour changes to violet and then to red. Catechol, like the other dihydric phenols, has well-marked acid properties.

Resorcinol, *metadihydroxy-benzene,* 1 : 3-$C_6H_4(OH)_2$.—This substance is prepared by the fusion with potash of benzene metadisulphonic acid (p. 181). It is a crystalline solid which dissolves readily in water, and gives a violet coloration with ferric chloride. It is used in the manufacture of many dyes; for example, of fluorescein and eosin.

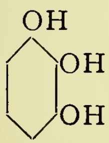
Quinol, *paradihydroxy-benzene,* 1 : 4-$C_6H_4(OH)_2$.—This substance is usually prepared by the reduction of quinone, $C_6H_4O_2$ (p. 169), by means of sulphurous acid—

$$\underset{\text{Quinone}}{C_6H_4O_2} + H_2O + H_2SO_3 = \underset{\text{Quinol}}{C_6H_4(OH)_2} + H_2SO_4.$$

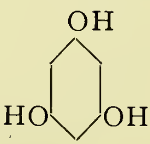
Like the other dihydric phenols, it dissolves readily in water, and its solution on addition of ferric chloride gives a green coloration, which almost immediately changes to yellow. The green coloration is that due to quinol, and the change to yellow is due to the oxidation by ferric salt of quinol to quinone, which has a bright yellow colour. On account of its mild reducing properties, an alkaline solution of quinol is extensively used as a photographic developer.

Trihydric Phenols.

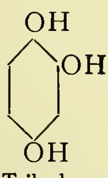
There are three trihydric phenols which possess the following formulæ:—



Pyrogallol (Pyrogallic acid)



Phloroglucinol



1 : 2 : 4-Trihydroxy-benzene

Pyrogallol, 1 : 2 : 3-$C_6H_3(OH)_3$.—This substance is prepared by heated gallic acid (p. 173), which at 200° gradually loses carbon dioxide, according to the following equation—

$$\underset{\text{Gallic acid}}{C_6H_2(OH)_3 . COOH} = \underset{\text{Pyrogallic acid}}{C_6H_3(OH)_3} + CO_2.$$

It may be purified by sublimation, when it forms a very light crystalline mass, or by recrystallisation. It is very soluble in water, and its solution gives a purple coloration with ferric chloride. When alkali is added to its aqueous solution, the alkaline salt thus produced has the property of readily absorbing oxygen gas. Alkaline pyrogallol is therefore much used in gas analysis as an absorbent for oxygen. Pyrogallol itself has marked reducing properties, and is used in feebly alkaline solution as a photographic developer.

Phloroglucinol, 1 : 3 : 5-$C_6H_3(OH)_3$, or symmetrical trihydroxy-benzene, is produced in the form of a potassium salt when gamboge or a similar resinous substance is fused with potash. It is a colourless solid which is very soluble in water, the aqueous solution having a sweet taste. It gives a violet coloration with ferric chloride.

The third isomer, or 1 : 2 : 4-trihydroxy-benzene, is of little importance.

PHENOL ETHERS.

When the hydrogen of the hydroxyl group of an alcohol is replaced by an alkyl radical, the resulting substance is an ether. Thus if we replace the hydroxylic hydrogen of ethyl alcohol by the radical methyl we obtain ethyl-methyl ether—

$$\underset{\text{Ethyl alcohol}}{C_2H_5 . O . H.} \qquad \underset{\text{Ethyl-methyl ether}}{C_2H_5 . O . CH_3.}$$

If, on the other hand, we replace the hydroxylic hydrogen of an acid by an alkyl radical we obtain, not an ether, but an ester. Thus by replacing the hydrogen of acetic acid by methyl we obtain the ester methyl acetate—

$$\underset{\text{Acetic acid}}{CH_3 . CO . OH.} \qquad \underset{\text{Methyl ester of acetic acid}}{CH_3 . CO . COCH_3.}$$

Consider, now, what would occur if the hydroxylic hydrogen of

a phenol were replaced by an alkyl such as methyl. As we have seen, phenol presents certain properties of an alcohol, but it also presents certain properties of an acid. If, therefore, the hydrogen were replaced by methyl we should be at a loss to determine by analogy whether to class the resulting substance as an ether or as an ester. There is, however, a practical test by means of which ethers and esters may, in most cases, be readily distinguished. Esters are in general readily saponified by alkalies, whilst ethers are not. If we apply this practical test to the alkyl derivatives of phenol, the alkyl replacing the hydrogen of the hydroxyl group, we find that they are not saponified by means of alkali, and therefore we class them as ethers and not as esters.

The mode of formation of these phenol ethers is analogous to one method for preparing the ordinary ethers. If we evaporate a solution of phenol in caustic soda we obtain a residue of sodium phenoxide. If this substance is heated with methyl iodide or dimethyl sulphate, double decomposition occurs, as represented in the following example—

$$C_6H_5.O.Na + (CH_3)_2SO_4 = \underset{\text{Anisole}}{C_6H_5.O.CH_3} + CH_3NaSO_4.$$

Anisole, *methoxy-benzene*, $C_6H_5.O.CH_3$, or phenyl-methyl ether, prepared in this way, is a colourless liquid possessing a characteristic odour. It has none of the properties of a phenol. When heated with a concentrated solution of hydriodic acid, it is decomposed with formation of phenol and methyl iodide—

$$C_6H_5.O.CH_3 + HI = CH_3I + C_6H_5.OH.$$

Methoxy-derivatives of aromatic substances are of frequent occurrence in nature, especially amongst the alkaloids and similar vegetable active principles. They can be all decomposed in the same way as anisole by the action of concentrated hydriodic acid, with formation of methyl iodide and a phenolic substance. Several instances of them will be met with later.

Guaiacol, *o*-$C_6H_4(OCH_3)(OH)$, has already been mentioned as the source of catechol (p. 164). It is both a phenol ether in virtue of the methoxy group, and a phenol in virtue of the hydroxy group. It is found in beechwood tar, and is employed

on account of its antiseptic properties in the treatment of phthisis. It is generally met with as a colourless liquid with a smell resembling that of wood creosote, but when pure it is a crystalline solid which melts at 28°.

AROMATIC KETONES AND QUINONES.

When calcium acetate is heated in absence of air it breaks up into calcium carbonate and acetone or dimethyl ketone—

$$\begin{matrix} CH_3.COO \\ CH_3.COO \end{matrix}\!\!>\!Ca = \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CO + CaCO_3.$$

Similarly, when calcium benzoate is heated in absence of air, it decomposes, with formation of calcium carbonate and diphenyl ketone, or **benzophenone**—

$$\begin{matrix} C_6H_5.COO \\ C_6H_5.COO \end{matrix}\!\!>\!Ca = \underset{\text{Benzophenone}}{\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix}\!\!>\!CO} + CaCO_3.$$

Benzophenone is a typical aromatic ketone, and resembles the fatty ketones in its general properties.

If a mixture of calcium benzoate and calcium acetate (containing possibly a mixed salt) is heated, then besides the two simple ketones, acetone and benzophenone, a mixed ketone, namely, methyl-phenyl ketone, is produced at the same time—

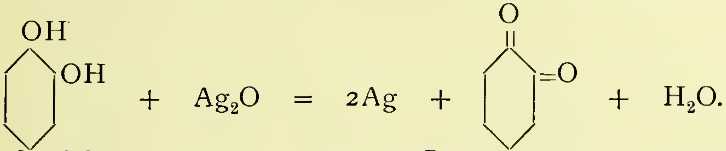
$$\begin{matrix} C_6H_5.COO \\ CH_3.COO \end{matrix}\!\!>\!Ca = \underset{\text{Acetophenone}}{\begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\!\!>\!CO} + CaCO_3.$$

This substance contains both an alkyl radical and an aromatic radical. It is termed **acetophenone**, and may be obtained in the form of crystals which melt at 20°. It is sometimes used in medicine as a hypnotic, under the name of **hypnone.**

Quinones are a special kind of double ketones, peculiar to the aromatic series, and are of two types, the orthoquinones and the paraquinones. The latter are of much more frequent occurrence.

If catechol is oxidised by means of silver oxide, it loses two

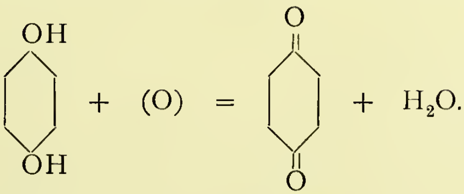
atoms of hydrogen and is converted into the orthoquinone of benzene, which crystallises in bright red plates but is not stable—



Catechol Benzene *o*-quinone

This quinone may be reduced again to catechol by means of sulphurous acid.

Quinone, $C_6H_4O_2$.—The ordinary quinone derived from benzene has the oxidised carbons in the para position with regard to each other. As has already been stated, it may be derived from parahydroxy-benzene or quinol by oxidation—

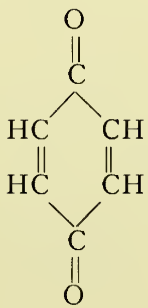


Quinol Quinone

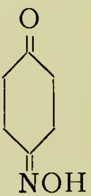
It is generally prepared, however, by the oxidation of aniline, $C_6H_5 . NH_2$, with chromic acid mixture, the oxidising process being here of a somewhat complicated nature, although easily carried out in practice.

Quinone occurs in the form of yellow crystals, which melt at 116° and can be purified by sublimation. It possesses a characteristic odour, and is only sparingly soluble in cold water. On reduction it passes into quinol.

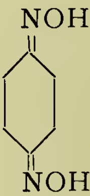
The complete graphic formula of quinone is usually written as follows:—



It will be noticed that the arrangement of the carbon valencies in the formula of quinone cannot be the same as the arrangement in benzene and its ordinary derivatives, if we assume that the group $>C=O$ exists in the compound. If quinone contains two carbonyl groups, it might be expected to react with hydroxylamine as a double ketone. This it does, and by the action of hydroxylamine upon it there may be derived the two substances quinone monoxime and quinone dioxime, the formulæ of which are given below—



Quinone monoxime



Quinone dioxime

The behaviour of quinone towards bromine seems to indicate that it in reality contains two unsaturated ethylene groups, as is indicated in the above formula, since it combines directly with four atoms of bromine to form quinone tetrabromide.

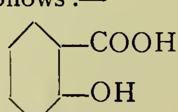
The point in which the quinones differ in structure from the aromatic ketones proper is, that the carbonyl groups which they contain form part of the ring or closed chain, whereas in the ketones like benzophenone the carbonyl group is external to the aromatic nucleus.

All quinones are coloured, and one theory of the connection between chemical structure and the existence of colour assumes that all coloured organic substances have what is called quinonoid structure.

PHENOLIC ACIDS AND ALCOHOLS.

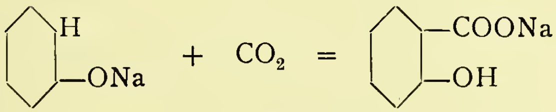
Salicylic Acid.

Salicylic acid is orthohydroxy-benzoic acid, and is at once an ordinary carboxylic acid and a phenol. Its graphic formula may be represented as follows :—



Salicylic acid

It occurs in the form of the methyl ester in oil of wintergreen, and may be obtained from the glucoside, salicin, which is found in willow bark (p. 211). It is generally prepared, however, from phenol by the following process :—The phenol is converted into sodium phenolate, which is then heated to 140° with carbon dioxide under pressure. The reaction which occurs is ultimately one of addition, with formation of sodium salicylate—

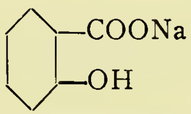


From this salt salicylic acid may be liberated by the addition to its solution of a strong mineral acid.

Salicylic acid occurs in the form of a white crystalline substance which melts at 156°, and may be sublimed at a somewhat higher temperature. It is sparingly soluble in cold water (1 in 450), much more soluble in hot water (about 1 in 13). It may therefore easily be purified by recrystallisation from boiling water. Many of its reactions resemble those of phenol; for example, it gives a precipitate with bromine water and a violet coloration with ferric chloride. Its solution, however, may be easily distinguished from that of phenol, as it possesses no odour.

Since salicylic acid contains a phenolic hydroxyl group it has well-marked antiseptic properties, to which it owes its use in medicine and also as a preservative. Its employment as a preservative in food-stuffs is in most countries either forbidden, or under strict regulation as to quantity, owing to its decided physiological action.

Sodium salicylate is frequently employed in medicine. It has the formula—



Sodium salicylate

only the hydrogen of the hydroxyl group being replaced by sodium. It crystallises well, is very soluble in water, and possesses a characteristic sweetish taste.

When sodium salicylate is heated with excess of solid caustic soda, or with soda lime, it yields phenol, which can readily be recognised by its odour—

$$C_6H_4\left\langle\begin{matrix}COONa\\ OH\end{matrix}\right. + NaOH = C_6H_5.OH + Na_2CO_3.$$

This action is, in a sense, the reverse of the synthetic formation of salicylic acid from phenol.

Some salts are known in which a metal takes the place of both of the replaceable hydrogens. Thus, when salicylic acid is heated with lime water it yields the salt—

$$C_6H_4\left\langle\begin{matrix}COO\\ \\ O\end{matrix}\right\rangle Ca,$$

by means of which it may be separated from the other isomeric hydroxy-benzoic acids, which do not yield corresponding salts.

Salol, *phenyl salicylate,* $C_6H_4\left\langle\begin{matrix}COOC_6H_5\\ OH.\end{matrix}\right.$ When salicylic acid is heated at 220°, two molecules of it lose water and carbon dioxide, with formation of phenyl salicylate or salol—

$$2C_6H_4\left\langle\begin{matrix}COOH\\ OH\end{matrix}\right. = C_6H_4\left\langle\begin{matrix}COOC_6H_5\\ OH\end{matrix}\right. + CO_2 + H_2O.$$

This substance still contains a phenolic hydroxyl, and is used as an intestinal antiseptic.

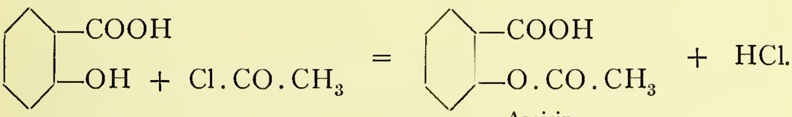
Methyl salicylate, $C_6H_4\left\langle\begin{matrix}COOCH_3\\ OH.\end{matrix}\right.$ It has already been stated that this substance is the main constituent of oil of wintergreen. It is artificially obtained by heating salicylic acid and methyl alcohol with a little concentrated sulphuric acid—

$$C_6H_4\left\langle\begin{matrix}COOH\\ OH\end{matrix}\right. + CH_3OH = C_6H_4\left\langle\begin{matrix}COOCH_3\\ OH\end{matrix}\right. + H_2O.$$

It has medicinal properties resembling those of salicylic acid

itself, and on account of its pleasant odour is also used as a perfume.

Aspirin, *acetyl-salicylic acid*, $C_6H_4\left\langle\begin{matrix}COOH\\ O.CO.CH_3.\end{matrix}\right.$ When salicylic acid is heated with acetyl chloride, the following action takes place:—



Aspirin

In the acetyl-salicylic acid thus formed the carboxyl group remains intact and the phenolic hydroxyl is converted into an acetate group. Aspirin consequently does not behave as a phenol, but when taken internally it is hydrolysed in the body, with production of salicylic acid.

Salicylic Alcohol, *o*-$C_6H_4(OH).CH_2OH$.

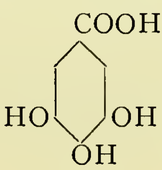
This substance exists in nature as a component of the glucoside **salicin** (p. 211). When salicin is hydrolysed by boiling with acidulated water it splits into glucose and salicylic alcohol, or **saligenin**, according to the following equation:—

$$\underset{\text{Salicin}}{C_{13}H_{18}O_7} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Saligenin}}{C_6H_4(OH).CH_2OH}.$$

Saligenin is at once a primary aromatic alcohol and a phenol, and it exhibits the actions of both types of substances. On oxidation it yields first salicylic aldehyde and then salicylic acid.

Gallic Acid, $C_6H_2(OH)_3COOH$.

This substance occurs in a considerable number of plants, but is generally prepared from tannin by boiling with acidulated water. Its graphic formula is as follows:—



It is sparingly soluble in cold water, but easily soluble in boiling water. It crystallises from aqueous solution with one molecule of water of crystallisation, which it loses on being gently heated. When heated to a little above 200° it decomposes with evolution of carbon dioxide, giving rise to pyrogallol—

$$C_6H_2(OH)_3COOH = C_6H_3(OH)_3 + CO_2.$$

In alkaline solution it absorbs oxygen from the air and turns brown. It gives a bluish black coloration with ferric chloride even in extremely dilute solutions. A basic gallate of bismuth is used as an antiseptic dusting powder, under the name of **dermatol.**

Tannin.

Tannin, sometimes called **tannic acid**, is a substance which occurs in considerable quantity in plants. Many barks contain it, and are used for the purpose of tanning leather. It is found in oak galls to the extent of half the weight of the dry substance. Tea also contains a considerable amount, and the astringent taste which the infusion acquires on long standing with the leaves is due to the tannin which is gradually dissolved out of them. Tannin is a practically colourless, apparently non-crystalline substance which readily dissolves in water, the solutions giving a deep bluish black colour with ferric chloride.

Different plants seem to yield slightly different varieties of tannin, and there is still some doubt as to its chemical constitution and even composition. When boiled with dilute acids tannin is hydrolysed, with production of gallic acid; and it was formerly assumed that tannin is digallic acid formed from two molecules of gallic acid with elimination of one molecule of water, as represented by the formula—

$$\underset{\text{Digallic acid}}{C_6H_2(OH)_3 . CO . O . C_6H_2(OH)_2 . COOH.}$$

Against this view of the nature of tannin there is a fact that it is an optically active substance. Since the formula of digallic acid contains no asymmetrical carbon atom, it probably does not represent the formula of tannin. It would appear from recent researches that the natural tannins are gallic acid esters of

glucose, which here plays the part of an alcohol in virtue of its numerous alcoholic hydroxyl groups. Since glucose is an optically active substance, the slight optical activity of tannin may thus be accounted for.

Tannin resembles gallic acid closely in its properties. Solutions of their alkaline salts absorb oxygen from the air, and can act as reducing agents. The colours given by ferric chloride are very similar. The two acids may be distinguished, however, by means of a solution of gelatin. This solution gives no precipitate with gallic acid, but readily yields a white precipitate with tannic acid.

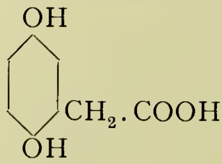
Tannic acid precipitates albumin solutions readily, and is therefore used in medicine as an astringent. Gallic acid is very slightly astringent.

The nature of the action of tannic acid (chiefly derived from oak bark) in tanning is not well known. It may be partly chemical, the tannin combining with the albuminous substance in the hide, or it may be mainly physical. The raw untanned hide when moist ferments and putrefies, and when dry becomes hard and horny. The tanned hide, on the other hand, shows no tendency to decomposition, and remains supple even when dry.

The tannin from oak galls is much used in the manufacture of **inks**, although the old iron and tannin inks have recently been largely superseded by solutions of aniline dyes. Ink may be made by adding a feebly acidulated solution of ferrous sulphate to a solution of tannin. The object of the acid is to prevent oxidation, tannin only oxidising readily when in alkaline solution. The solution has little colour, and is usually tinted artificially by means of some dye. When this solution has been applied to paper it dries in contact with the paper, and the small amount of acid which it contains is neutralised by the material with which the paper has been dressed. It therefore now oxidises in presence of atmospheric oxygen, and the ferrous iron becoming ferric, gives a deep blue-black compound which leaves a trace on the paper which is not liable to fade, and is not readily washed off on account of it being nearly insoluble in water. A little gum is usually added to prevent the ink from running too freely.

Homogentisic Acid, $C_6H_3(OH)_2CH_2 . COOH$.

This acid is a derivative of quinol, and has the formula—



Homogentisic acid

It is formed in the organism in the disease known as alcaptonuria. The urine in such cases darkens by oxidation when made alkaline and exposed to air.

CINNAMIC ACID DERIVATIVES.

Cinnamic aldehyde, $C_6H_5 . CH : CH . CO . H$.—This unsaturated aldehyde is found in oil of cinnamon, to which it gives the characteristic odour. It may be prepared by the condensation of acetaldehyde with benzaldehyde, according to the following equation :—

$$\underset{\text{Benzaldehyde}}{C_6H_5 . CH : O} + \underset{\text{Acetaldehyde}}{H_2CH . CO . H} = \underset{\text{Cinnamic aldehyde}}{C_6H_5 . CH : CH . CO . H} + H_2O.$$

On oxidation it yields the corresponding acid, cinnamic acid.

Cinnamic acid, $C_6H_5 . CH : CH . COOH$, occurs either free or in the form of esters in storax and in balsam of Tolu. It is generally prepared by heating a mixture of benzaldehyde, sodium acetate, and acetic anhydride. It would appear that benzaldehyde takes up the elements of sodium acetate in the ordinary way, to produce the sodium salt of phenyl-β-hydroxy-propionic acid—

$$C_6H_5 . \overset{O}{C} . H + CH_3 . COONa = C_6H_5 . \begin{array}{l} OH \\ | \\ C . H \\ | \\ CH_2 . COONa. \end{array}$$

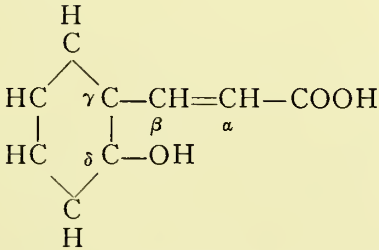
This salt loses water under the influence of the anhydride, and the unsaturated substance sodium cinnamate is produced—

$$C_6H_5 . CH(OH) . CH_2 . COONa = C_6H_5 . CH : CH . COONa + H_2O.$$

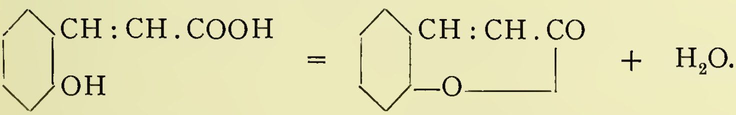
This method of synthesis of unsaturated acids from an aromatic aldehyde, a sodium salt, and an anhydride is called Perkin's synthesis. Cinnamic acid may also be prepared on a large scale by heating benzal chloride, $C_6H_5CHCl_2$, with sodium acetate. It is a crystalline substance moderately soluble in water, and is used in medicine both in the form of free acid and of the sodium salt.

If we consider cinnamic acid as a derivative of an unsaturated fatty acid, we see that it is β-phenyl-acrylic acid. An isomeric acid, α-phenyl-acrylic acid, $CH_2 : C(C_6H_5) . COOH$, **atropic acid**, may be obtained from the alkaloid atropine (p. 309).

Cumaric acid, o-$HO . C_6H_4 . CH : CH . CO_2H$.—This acid is the orthohydroxy-derivative of cinnamic acid. Its graphic formula is as given below—



From this formula it may be seen that the acid is a δ-hydroxy acid. Now we have already learnt that γ- and δ-hydroxy acids readily lose water and are converted into lactones. This is the case with cumaric acid, which readily loses water and is converted into the δ-lactone, cumarin—



Cumaric acid

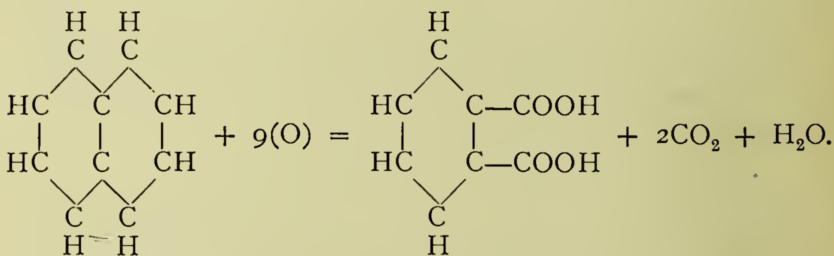
Cumarin
(Cumaro-lactone)

Cumarin is the odorous principle found in woodruff, certain forms of clover, and the tonka bean. It can be obtained synthetically, by means of Perkin's synthesis, from salicylic acid, sodium acetate, and acetic anhydride.

DIBASIC AROMATIC ACIDS.

Phthalic Acid, $C_6H_4(COOH)_2$.

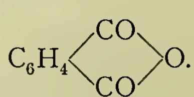
One of the principal hydrocarbons obtained in the distillation of coal-tar is naphthalene. This hydrocarbon contains two benzene rings, two atoms of carbon being common to both rings. When it is oxidised one of the benzene rings is split, with formation of two molecules of carbon dioxide and phthalic acid—



Naphthalene Phthalic acid

The oxidising agent used for this purpose is concentrated sulphuric acid, mercuric sulphate being used as catalyst. The sulphuric acid is reduced to sulphur dioxide. It should be noted that prolonged boiling with concentrated sulphuric acid, especially in presence of mercuric sulphate or copper sulphate, oxidises many organic substances, and is a process frequently used in organic chemistry, especially in physiological analysis for the estimation of nitrogen by means of Kjeldahl's process.

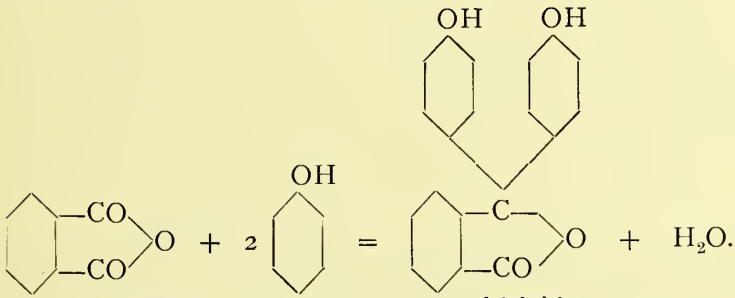
Phthalic acid is comparatively soluble in boiling water, but only sparingly soluble in cold water, so that it may readily be purified by crystallisation. It will be seen on reference to its formula that it is an orthodibasic acid, and therefore resembles succinic acid in having two carboxyl groups on neighbouring carbon atoms. Like succinic acid, it readily loses water on heating, and is converted into the corresponding **phthalic anhydride**—



The isomeric meta- and paradehydroxy-benzoic acids are of little importance.

Phenolphthalein.

When phthalic anhydride is heated with phenol and a dehydrating agent, the following reaction takes place:—



Phthalic anhydride Phenol Phenolphthalein

The hydrogen of the phenol which takes part in this reaction is the hydrogen in the para position to the hydroxyl group. The substance so produced is called phenolphthalein. In acid or neutral solution it is colourless, but in presence of alkalies it turns to a bright pink colour, and is therefore much used as an indicator. Phenolphthalein is related to an important class of dyes which will be referred to later (p. 316). It is extensively used as a purgative under various proprietary names, such as **purgen**, **laxin**, etc.

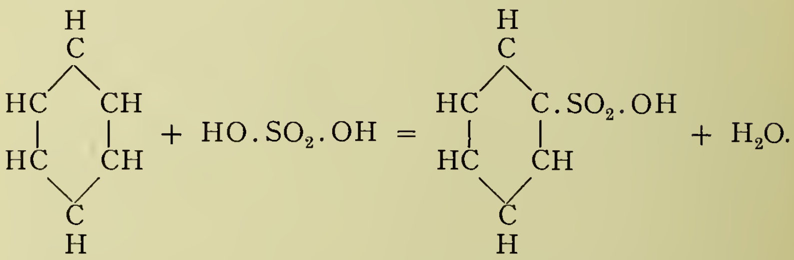
SULPHONIC ACIDS.

Concentrated, or even fuming, sulphuric acid has little action on the saturated fatty hydrocarbons. The unsaturated fatty hydrocarbons, such as ethylene, on the other hand, are readily dissolved by sulphuric acid, with formation of alkyl hydrogen sulphates. Thus ethylene itself gives rise to ethyl hydrogen sulphate—

$$\underset{\text{Ethylene}}{C_2H_4} + H_2SO_4 = \underset{\text{Ethyl hydrogen sulphate}}{C_2H_5.HSO_4}$$

The action of concentrated sulphuric acid on aromatic hydrocarbons is quite different from its action on ethylene. If benzene and concentrated sulphuric acid are warmed together for a considerable period, the benzene gradually dissolves, and an acid named **benzene-sulphonic acid** is found in the resulting

liquid. The equation for the formation of this acid is as follows :—



Benzene-sulphonic acid

It will be noticed that this sulphonic acid contains only three atoms of oxygen. It cannot, therefore, be analogous to sulphovinic acid, $C_2H_5 . HSO_4$, which contains four oxygen atoms. It might, however, so far as its composition is concerned, be looked upon as an acid sulphite. That this is not a correct view of its composition is indicated by the fact that isomeric substances are known which are true sulphites and have entirely different properties from the sulphonic acids of the same composition. The difference seems to be that in true sulphites the organic radical is directly united to oxygen, whereas in sulphonic acids it is directly united to sulphur.

The aromatic sulphonic acids are much stronger than aromatic carboxylic acids. Benzene-sulphonic acid is almost as powerful as strong mineral acids such as hydrochloric or nitric acids. The sulphonic acids may be separated from any excess of sulphuric acid used in their formation by taking advantage of the fact that their calcium and barium salts are freely soluble in water, whilst the corresponding sulphates are insoluble. The sulphonic acids themselves are generally crystalline substances which are soluble in water.

The most important reaction which they exhibit is that produced on fusion with an alkali. Thus, when sodium benzene-sulphonate is fused with excess of caustic soda, it reacts according to the following equation :—

$$\underset{\text{Sodium benzene-sulphonate}}{C_6H_5 . SO_2 . ONa} + NaOH = \underset{\text{Phenol}}{C_6H_5 . OH} + \underset{\text{Sodium sulphite}}{Na_2SO_3},$$

with production of sodium sulphite and phenol. The sulphonic

acids are therefore frequently employed as intermediate substances in the conversion of hydrocarbons into phenols. The hydrocarbon is first converted into a sulphonic acid by means of concentrated or fuming sulphuric acid, and this sulphonic acid is afterwards fused with excess of caustic alkali, yielding the hydroxyl group in place of the original hydrogen which was attacked by the sulphuric acid. The oxidising agent in this case is concentrated sulphuric acid, which is ultimately reduced by the action of the hydrocarbon to a sulphite.

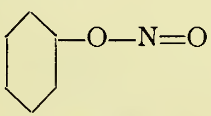
When more than one sulphonic group is introduced into an aromatic nucleus, the groups take up the meta position with respect to each other. Thus the only disulphonic acid produced directly from benzene and sulphuric acid is *m*-benzene-disulphonic acid, 1 : 3-$C_6H_4(SO_3H)_2$, used in the preparation of resorcinol (p. 165).

AROMATIC NITRO COMPOUNDS.

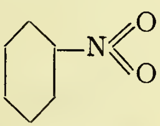
Whilst nitric acid has little effect on the saturated fatty hydrocarbons, it reacts readily with the hydrocarbons of the benzene series in much the same way as concentrated sulphuric acid. The hydroxyl group of the acid unites with a hydrogen atom of the aromatic ring to form water, and the residual nitro group NO_2 of the nitric acid takes the place of the hydrogen atom. Thus from benzene itself and concentrated nitric acid are obtained nitrobenzene—

$$C_6H_6 + HO.NO_2 = \underset{\text{Nitrobenzene}}{C_6H_5.NO_2} + H_2O.$$

It will be observed, that as benzene-sulphonic acid is isomeric with phenyl hydrogen sulphite, so here nitrobenzene is isomeric with phenyl nitrite. The difference in constitution is expressed by the formulæ—



Phenyl nitrite



Nitrobenzene

In phenyl nitrite the phenyl group is directly united to oxygen in nitrobenzene it is united to nitrogen.

The nitro substitution products of the aromatic series are very stable bodies, and are not hydrolysed by boiling with alkaline solutions. They must be carefully distinguished from such substances as "nitroglycerine," which is not truly a nitro substance at all, but an organic nitrate containing the group $.O.NO_2$, and easily saponifiable. Nitro groups, like sulphonic groups, take up the meta position with respect to one another.

Their chief use is in the manufacture of explosives, and as intermediate substances in the preparation of aromatic bases, the nitro group NO_2 being easily reduced to the amino group NH_2, *e.g.*—

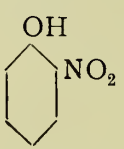
$$\underset{\text{Nitrobenzene}}{C_6H_5.NO_2} + 6(H) = \underset{\substack{\text{Aminobenzene}\\\text{(Aniline)}}}{C_6H_5.NH_2} + 2H_2O.$$

In the process of nitration concentrated sulphuric acid is frequently used in conjunction with concentrated nitric acid, as the action of the latter then proceeds more rapidly.

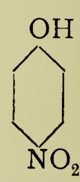
When one hydrogen atom of the aromatic hydrocarbon has already been replaced, the nitrating action often takes place with great ease. Thus phenol may be nitrated with dilute nitric acid, and it is possible to get one, two, or three nitro groups into the phenol molecule without difficulty.

Nitrobenzene, $C_6H_5.NO_2$, is a pale yellow liquid which freezes at 5° and boils at 208°. It has a characteristic odour, resembling that of oil of bitter almonds (benzaldehyde), for which it is sometimes used as a substitute.

Nitrophenols, $C_6H_4(OH).NO_2$.—A mixture of ortho- and paranitrophenols is produced when phenol is nitrated with diluted nitric acid in the cold—



o-Nitrophenol

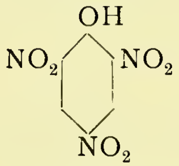


p-Nitrophenol

Both are solids, the ortho compound being yellow and the para compound colourless. They are stronger acids than phenol itself, and the solutions of their salts are intensely yellow. For

this reason they are sometimes used as indicators in acidimetry instead of methyl orange.

Picric acid, *trinitrophenol*, $C_6H_2(OH)(NO_3)_3$.—This substance is produced by the action of concentrated nitric acid on phenol. Its graphic formula is—



Picric acid

It is also formed when concentrated nitric acid acts on many other substances—*e.g.*, wool, resins, leather.

Picric acid is a pale yellow crystalline substance, but in aqueous solution it has a deep yellow colour, and readily stains nitrogenous fibres such as silk or wool. It is almost as powerful an acid as hydrochloric acid, although it is a phenol, and not a true carboxylic acid. The increase in strength is due to the accumulation of nitro groups in the molecule. Its salts crystallise well and are usually explosive. The acid is safe to handle as loose crystals, but when these are melted together and allowed to solidify, the mass forms a powerful explosive when fired by means of a detonator. The military explosive **lyddite** consists of picric acid, and the acid itself and its salts enter into the composition of many explosive mixtures. The empirical formula $C_6H_3N_3O_7$ shows that there is practically just enough oxygen in the molecule to convert the carbon into carbon monoxide and the hydrogen into water, so that a large volume of gas is generated on its explosion.

NAPHTHALENE AND ITS OXYGEN DERIVATIVES.

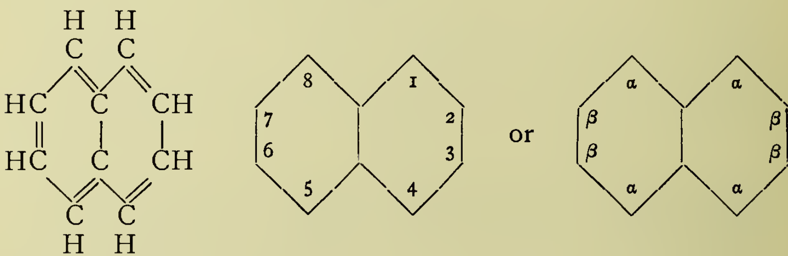
It has been stated in the previous chapter that naphthalene is one of the chief hydrocarbons derivable from coal-tar. An indication of the method of extraction has already been given.

Naphthalene, $C_{10}H_8$.

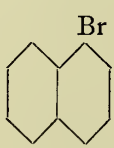
Naphthalene crystallises in plates which melt at about 80°. It sublimes readily, and even at the ordinary temperature gives

off vapour which possesses a characteristic smell, by means of which it may be easily identified. It is used in medicine as a disinfectant, and is also employed for preserving furs, clothing, etc., from the attacks of moths.

The graphic formula of naphthalene is generally written in one or other of the following ways:—



In the first formula all the atoms constituting the molecule are indicated. There is the same doubt as to the position of the double or blank bonds as there is in the case of benzene. The second and third formulæ correspond to the plain hexagon formula for benzene. The second gives the carbon atoms as they are usually numbered, in order that various isomers may be readily distinguished from each other. The third formula distinguishes between the two kinds of hydrogen atoms considered from the point of view of their relationship to the whole molecule. It is obvious that the four hydrogens marked α differ in their relationship to the molecule of the hydrogen atoms marked β. It is thus possible to have two mono-derivatives of naphthalene instead of the single derivative possible in the case of benzene; and we distinguish, therefore, between, say, α-bromonaphthalene and β-bromonaphthalene, which have the following formula:—



α-Bromonaphthalene

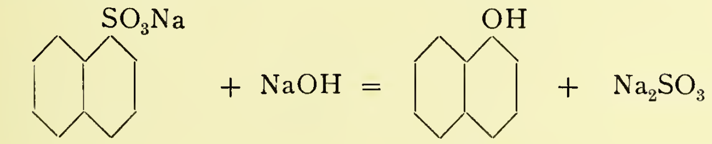
β-Bromonaphthalene

When naphthalene is warmed with fuming sulphuric acid at a temperature of about 80°, a mixture of α-naphthalene-

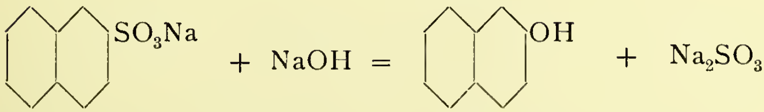
sulphonic acid and β-naphthalene-sulphonic acid is obtained. When the sulphonation is carried out at a higher temperature in the neighbourhood of 200°, the β acid alone is produced. The equation representing the formation of these acids is as follows:—

$$C_{10}H_8 + H_2SO_4 = \underset{\text{Naphthalene-sulphonic acid}}{C_{10}H_7.SO_3H} + H_2O.$$

When fused with excess of caustic alkali the sulphonic acids yield the corresponding naphthols, thus:—



α-Naphthol

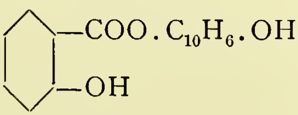


β-Naphthol

The α- and β-naphthols resemble phenols in their properties. They are very sparingly soluble in water, but readily soluble in alkaline solutions, with formation of alkaline salts corresponding to the phenoxides. They have marked antiseptic properties, and are used as antiseptic substances in medicine.

α-Naphthol, $C_{10}H_7.OH$, melts at 95°, and by the action of nitric acid is easily converted into a dinitro-derivative which, like picric acid derived from phenol, is a comparatively powerful acid. The sodium salt of this dinitro-α-naphthol is used as a dye, and is known as naphthalene yellow.

β-Naphthol, $C_{10}H_7.OH$, melts at 122°, and is more extensively used in medicine that α-naphthol. β-Naphthol salicylate, which has the following formula:—



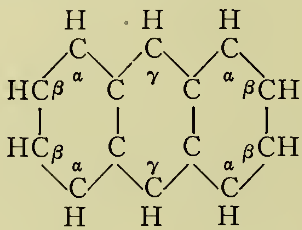
has similar properties to salol, and is employed in medicine under the name **betol**.

ANTHRACENE AND ITS OXYGEN DERIVATIVES.

The hydrocarbon **anthracene**, $C_{14}H_{10}$, is found in the higher-boiling portions of the distillate from coal-tar. It crystallises readily, and may be purified from the crude product partly by distillation and partly by recrystallisation.

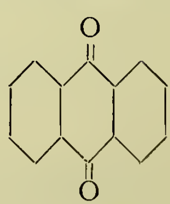
Anthracene occurs in the form of colourless plates, which show a marked blue fluorescence. It melts at 216°, and boils at 351°. It does not dissolve in water, and is little soluble in alcohol or ether. It dissolves readily, however, in hydrocarbon solvents such as benzene.

Its graphic formula is represented as follows :—



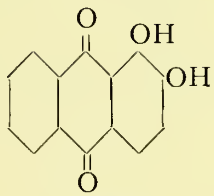
Three mono-derivatives of anthracene are possible. The α- and β-derivatives correspond to those of naphthalene; the γ-derivative has the substituting radical on a carbon atom of the middle ring. The γ-carbon atoms differ markedly in their behaviour from the α- and β-carbon atoms inasmuch as they are readily oxidised. Thus, when anthracene is treated with chromic acid or with nitric acid it is converted into anthraquinone.

Anthraquinone, $C_{14}H_8O_2$, is a paraquinone, but differs from the paraquinone derived from benzene in possessing a much paler colour, in being without odour, and in not being so readily reduced to a hydroxy compound. Many important dyes are derivatives of anthraquinone, which has the following formula :—



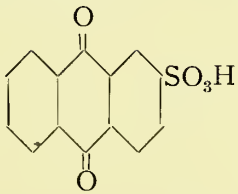
Anthraquinone

Alizarin is a dihydroxy-anthraquinone of the following constitution :—

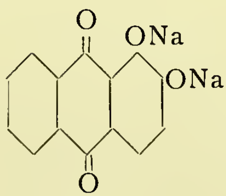


Alizarin

It occurs naturally in madder in the form of a glucoside, and is used in turkey-red dyeing. It is prepared from anthracene by first oxidising the hydrocarbon to anthraquinone, which is then converted by heating with fuming sulphuric acid into anthraquinone-β-sulphonic acid—



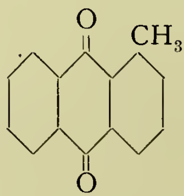
When the sodium salt of this acid is fused with caustic soda and potassium chlorate, a hydroxy group takes the place of the sulphonic acid group, and at the same time the neighbouring α-hydrogen atom is oxidised by the chlorate to a second hydroxy group, so that in presence of the excess of alkali the sodium salt of alizarin—



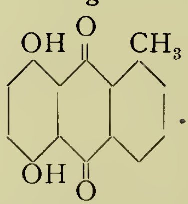
is produced. Alizarin is liberated from this sodium salt by means of dilute sulphuric acid. It may be purified by sublimation, and forms orange-yellow needles which melt at 289°. It is practically insoluble in water, but on account of the phenolic groups it dissolves readily in alkalies. It owes much of its utility as a dye to the fact that it forms brightly coloured

insoluble compounds with many metallic hydroxides. Thus, if alizarin is added to a solution of an aluminium salt which is then precipitated by means of ammonia, the precipitate which is obtained is of a bright crimson colour.

The purgative substances existing in senna, cascara sagrada, and rhubarb root are polyhydroxy-derivatives of **α-methyl-anthraquinone**—

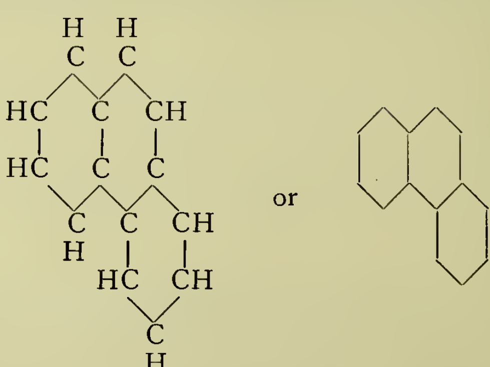


They probably occur for the most part in plants as glucosides. For instance, rhubarb contains a glucoside of **chrysophanic acid**—



Phenanthrene, $C_{14}H_{10}$.

Phenanthrene is found along with its isomeride anthracene in anthracene oil. Its formula is written as follows :—



It resembles anthracene in its properties, and is important as being the parent substance of certain opium alkaloids.

SUGARS.

The natural sugars and those that have been prepared artificially belong to one of two classes. They are either hydroxy-aldehydes or hydroxy-ketones. Since the termination *ose* is employed in the case of all carbohydrates, the aldehyde sugars are conveniently called **aldoses**, and the ketone sugars **ketoses**. In all sugars proper the carbon which is attached to the hydroxyl group is also directly united to the carbonyl group of the aldehyde or ketone.

It is possible to obtain sugars with varying numbers of carbon atoms, and sugars may be classified from this point of view. First of all we have the simple sugars, containing only one aldehyde group or one ketone group. Such a simple sugar may be termed a diose, triose, tetrose, pentose, hexose, according as it contains two, three, four, five, or six oxidised carbon atoms. The principal natural sugars contain either six carbon atoms or a multiple of six.

The simplest substance which corresponds to the above definition of a sugar is **glycollic aldehyde**, $CH_2(OH).CO.H$. This substance is intermediate between glycol and glycollic acid—

$\begin{array}{l} CH_2.OH \\ \vert \\ CH_2.OH \end{array}$	$\begin{array}{l} CH_2.OH \\ \vert \\ CO.H \end{array}$	$\begin{array}{l} CH_2.OH \\ \vert \\ CO.OH \end{array}$
Glycol	Glycollic aldehyde	Glycollic acid

It is an aldose, and possesses the characteristic properties of the simple sugars; namely, it reduces Fehling's solution, is coloured yellow by alkalies, and yields an osazone with phenyl-hydrazine (p. 194).

As the simplest ketone must contain at least three carbon atoms, the simplest ketose is necessarily a triose, and is the substance known as **dihydroxy-acetone**—

$CH_3.CO.CH_3$	$CH_2(OH).CO.CH_2(OH)$
Acetone	Dihydroxy-acetone

This substance is isomeric with **glyceric aldehyde**, an aldose intermediate between glycerol and glyceric acid—

$$\begin{array}{lll}
CH_2.OH & CH_2.OH & CH_2.OH \\
| & | & | \\
CH.OH & CH.OH & CH.OH \\
| & | & | \\
CH_2.OH & CO.H & CO.OH \\
\text{Glycerol} & \text{Glyceric aldehyde} & \text{Glyceric acid}
\end{array}$$

It will be observed that the formula of glycollic aldehyde is $C_2H_4O_2$, and the formula of glyceric aldehyde and dihydroxy-acetone, $C_3H_6O_3$. All these substances, then, have the composition corresponding with that of a carbohydrate as originally understood; that is, the oxygen and hydrogen contained in them are exactly in the proportions necessary for the formation of water. The tetroses, $C_4H_8O_4$, are of little importance. Some pentoses, $C_5H_{10}O_5$, occur in nature; of these may be mentioned **arabinose**, which occurs in gum arabic, and **xylose**, which may be obtained by boiling bran, straw, pine wood, etc., with dilute hydrochloric acid. Both of these sugars are aldoses.

As has already been said, the hexoses, $C_6H_{12}O_6$, are by far the most important class of sugars. The chief natural representatives are **glucose**, which is an aldohexose, and **fructose**, which is a ketohexose.

These simple sugars are known as **monosaccharides**. Other sugars exist, however, which are composed of two, three, or more of these simple units combined together with elimination of water. Such sugars are termed disaccharides, trisaccharides, etc. The chief representatives of the **disaccharides**, $C_{12}H_{22}O_{11}$, are cane-sugar or **sucrose**, malt-sugar or **maltose**, and milk-sugar or **lactose**. **Raffinose**, $C_{18}H_{32}O_{16}$, is an example of a **trisaccharide**, and is the main constituent of Australian manna. It should be noted that these polysaccharides may or may not be true sugars in the sense of our original definition, as it is possible that in the union of the two sugar units with elimination of water the aldehyde or keto group of both molecules may be changed. It is always possible by boiling a polysaccharide with dilute acid to hydrolyse and split it up into its constituent monosaccharides. Thus, when cane-sugar is boiled with dilute hydrochloric acid, it is hydrolysed and converted into a mixture of glucose and fructose. This particular

hydrolysis is often spoken of as the **inversion** of cane-sugar, and the mixture of glucose and fructose is conveniently known as **invert sugar.** The reason for the application of these terms is that whilst sucrose is dextro-rotatory, the mixture of equal quantities of glucose and fructose is lævo-rotatory, the specific lævo-rotation of fructose being greater than the specific dextro-rotation of glucose. Thus on hydrolysis the sign of rotation of cane-sugar is changed or inverted.

The following equation represents the inversion of cane-sugar, and the corresponding hydrolysis of milk-sugar and malt-sugar:—

$C_{12}H_{22}O_{11}$	+ H_2O =	$C_6H_{12}O_6$	+	$C_6H_{12}O_6$
Sucrose		Glucose		Fructose
Lactose		Glucose		Galactose
Maltose		Glucose		Glucose

It will be noticed that maltose on hydrolysis gives glucose alone, whereas the other disaccharides give a mixture of two different monosaccharides. The hydrolysis may be effected not only under the influence of acid as a catalyst, but also by specific enzymes, the **disaccharases,** the names *sucrase* or *invertase*, *lactase* and *maltase*, sufficiently indicating the relationship of the particular enzymes to the sugars on which they act. The condensation of the monosaccharides into disaccharides has also in some cases been effected by hydrochloric acid and by these enzymes.

STEREOCHEMISTRY OF THE HEXOSES.

If we write the graphic formula of an aldohexose, we see that it contains four asymmetric carbon atoms, all of which are dissimilar, thus—

$$
\begin{array}{rl}
 & \mathrm{H} \\
 & \mathrm{H.C.OH} \\
(1) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
(2) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
(3) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
(4) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \mathrm{H.C:O}
\end{array}
$$

Since each of the asymmetric carbon atoms may independently be either *d* or *l*, it follows that there are $2^4 = 16$ possible active isomers, arranged in eight pairs, each member of a pair being the optical opposite of the other. Most of these are known, the majority having been prepared artificially.

The stereochemistry of the ketohexoses is somewhat simpler. Thus in the formula—

$$\begin{array}{rc}
 & \mathrm{H} \\
 & \mathrm{H.C.OH} \\
(1) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
(2) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
(3) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \mathrm{C:O} \\
 & \mathrm{H.C.OH} \\
 & \mathrm{H}
\end{array}$$

there are only three asymmetric carbon atoms, so that the number of possible isomers is $2^3 = 8$, in four pairs of optical opposites.

There is a certain correspondence between the aldohexoses and ketohexoses. If the asymmetric carbon atoms marked (1), (2), and (3) in the above formulæ have the same stereochemical arrangement, or **configuration**, in both aldose and ketose, then the aldose and ketose are said to correspond. Ordinary glucose and fructose correspond in this way, for, as we shall see, it is possible to transform glucose into fructose without interfering with the configuration of the asymmetric carbon atoms (1), (2), and (3). No attempt is made in the above or similar formulæ to represent the configuration of the individual carbon atoms, although by a customary convention it is possible to do so.

Only those hexoses will receive mention here which are derived from the principal disaccharides by hydrolysis.

HEXOSES AND THEIR DERIVATIVES.

Glucose, $C_6H_{12}O_6$.

d-**Glucose,** also known as dextrose or grape-sugar, occurs in conjunction with fructose, in sweet fruits and in honey. The commercial preparation of the impure substance has been referred to on p. 56. In the laboratory it is most easily prepared by the inversion of cane-sugar, and by precipitation from the accompanying fructose by means of alcohol, glucose being much less soluble in concentrated alcohol than fructose. As the name dextrose implies, *d*-glucose is dextro-rotatory, and the concentration of its solutions may be estimated by means of the polarimeter (p. 123). It should be noted, however, that the rotation of a freshly prepared solution is nearly double that assumed by the same solution on keeping, or, more rapidly, on boiling. An explanation of this change in rotation is given below. The presence of glucose in diabetic urine is generally ascertained by its reducing action on Fehling's solution. The same reagent may be employed for the quantitative estimation of glucose, the weight of cuprous oxide precipitated by a known volume of the solution being ascertained. In interpreting the results of such experiments, other reducing substances must be proved absent or allowed for.

The action of phenyl-hydrazine on aldoses and ketoses is important, both from the point of view of the investigation of sugars, and from the point of view of detecting and discriminating them. This action may be illustrated for all aldoses, including glucose, by the following schemes, the active part of the aldose molecule being the aldehyde group and the secondary alcoholic group attached to it. The first action of the phenyl-hydrazine is on the aldehyde group, a **hydrazone** being produced in the usual way :—

$$\underset{\text{Aldose}}{\begin{array}{l} H.C.OH \\ \cdot \\ H.C:O \end{array}} + H_2N.NHC_6H_5 = \underset{\text{Phenyl-hydrazone}}{\begin{array}{l} H.C.OH \\ \cdot \\ H.C:N.NHC_6H_5 \end{array}} + H_2O$$

Phenyl-hydrazine, however, acts at the same time as an oxidising

agent, converting the secondary alcohol group into a ketone group:—

$$\begin{array}{l} H.C.OH \\ H.\dot{C}:N.NHC_6H_5 + H_2N.NHC_6H_5 = \\ \qquad\qquad\qquad\qquad C:O \\ \qquad\qquad\qquad H.\dot{C}:N.NHC_6H_5 + NH_3 + C_6H_5.NH_2 \end{array}$$

This ketone group is now attacked by a third molecule of phenyl-hydrazine, and a double hydrazone or **osazone** of the sugar is produced—

$$\begin{array}{l} C:O + H_2N.NHC_6H_5 \\ H.\dot{C}:N.NHC_6H_5 \end{array} = \underset{\text{Osazone}}{\begin{array}{l} C:N.NHC_6H_5 \\ H.\dot{C}:N.NHC_6H_5 \end{array}} + H_2O.$$

These osazones are usually crystalline substances, and, in contradistinction to the sugars, very sparingly soluble in water. They therefore separate in the crystalline state when the sugar solution is warmed to 100° for some time with phenyl-hydrazine, or a mixture of phenyl-hydrazine chloride and sodium acetate. **Phenyl-glucosazone** crystallises in bright yellow needles which are easily identified under a low power of the microscope by their characteristic form and mode of aggregation.

Since the hydroxylic hydrogen of an ordinary alcohol is under certain conditions replaceable by a metal, it is not surprising that this action should take place comparatively readily in the case of the sugars with their numerous hydroxyl groups and the aldehyde or keto group, which increase the acidic character of the hydroxyl. Thus we find that glucose forms with calcium hydroxide a compound, $C_6H_{11}O_5.O.Ca.OH$, called **calcium glucosate**, a basic calcium "salt" of glucose. This compound is moderately soluble in water, but its aqueous solution is at once decomposed when carbon dioxide is passed through it, the very feeble carbonic acid being sufficiently strong to effect its complete decomposition—

$$C_6H_{11}O_5.O.Ca.OH + CO_2 = CaCO_3 + C_6H_{12}O_6.$$

Reduction Products of Glucose.

The aldehydic group of glucose is capable of being reduced to a primary alcohol group by means of sodium amalgam. The product of reduction is the hexahydric alcohol **mannitol**—

$$\begin{array}{rc}
 & \mathrm{H} \\
 & \cdot \\
 & \mathrm{H.C.OH} \\
 & \cdot \\
(1) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \cdot \\
(2) & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \cdot \\
(2') & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \cdot \\
(1') & \mathrm{H.}\mathbf{C}\mathrm{.OH} \\
 & \cdot \\
 & \mathrm{H.C.OH} \\
 & \cdot \\
 & \mathrm{H}
\end{array}$$

Mannitol

d-**Mannitol**, $C_6H_{14}O_6$, is not only obtained as a reduction product of *d*-glucose, but is found in many plants, in particular in the juice of the manna-ash, which when dried constitutes manna. It is a crystalline substance easily soluble in water.

Like its isomerides, mannitol contains four asymmetric carbon atoms, but it will be noted that since here the two terminal groups of the molecule are the same, viz., primary alcohol groups, the number of possible isomers is not so great as with the aldohexoses; for now the asymmetric carbon atoms are similar in pairs, *i.e.* (1) and (1′), (2) and (2′), which limits the number of optically active isomerides to eight, but yields at the same time the possibility of two inactive modifications due to internal compensation.

Complete reduction of glucose produces normal hexane, which proves that the six carbon atoms are arranged as a straight chain.

Oxidised Products of Glucose.

Gluconic acid, $C_6H_{12}O_7$.—When *d*-glucose is carefully

oxidised with chlorine water it yields *d*-gluconic acid, the aldehyde group being oxidised to the carboxyl group—

$$\underset{d\text{-Glucose}}{HO.CH_2.(CHOH)_4.CO.H} + H_2O + Cl_2$$
$$= 2HCl + \underset{d\text{-Gluconic acid}}{HO.CH_2.(CHOH)_4.COOH}$$

The above equation holds good for the oxidisation of the sixteen possible aldehydes to sixteen corresponding isomeric acids. These acids are all monobasic, and have five alcohol groups in the molecule.

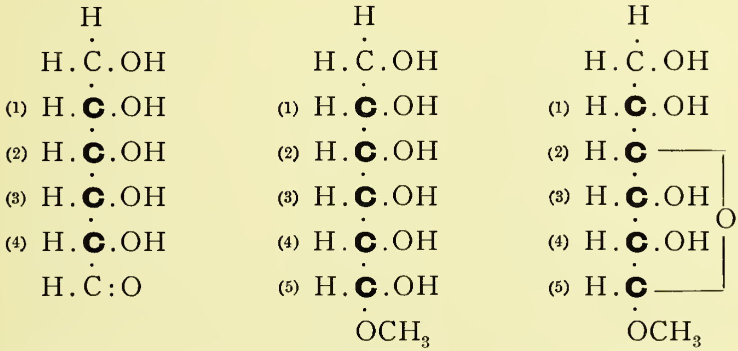
Saccharic acid, $HOOC.(CHOH)_4.COOH$.—Oxidation with nitric acid converts mannitol, glucose, or gluconic acid into the dibasic acid, saccharic acid, both the terminal groups of the carbon chain being oxidised to carboxyl groups. Saccharic acid is a very soluble deliquescent substance. The isomeric acid, **mucic acid**, which is obtained by the oxidation of galactose or milk-sugar, is a sparingly soluble crystalline substance. It is optically inactive by internal compensation. The isomerides correspond to those of mannitol in number and character.

Glycuronic acid, $H.CO.(CHOH)_4.COOH$.—The sodium salt of this aldehyde acid is obtained when saccharic acid is reduced by means of sodium amalgam. The acid occurs to a small extent in normal urine, and often more abundantly in pathological urine, combined with phenols and other substances. These condensed compounds, which resemble glucosides (see below), may be hydrolysed by boiling with dilute acid, and the glycuronic acid thus liberated. It should be noted that since glycuronic acid contains the group $CO.CH(OH)$, it reduces Fehling's solution.

Glucosides.

Glucose, being an aldehyde, displays a power of combining with compounds of the most diverse type, a hydrogen atom of the compound uniting with the oxygen of the CO group, and the rest of the molecule with the carbon of the same group. Thus, when methyl alcohol and glucose are warmed together in presence of anhydrous hydrochloric acid, union takes place

to form an addition compound, which, however, loses water with the hydroxyl group of the carbon and produces a substance known as methyl-glucoside—



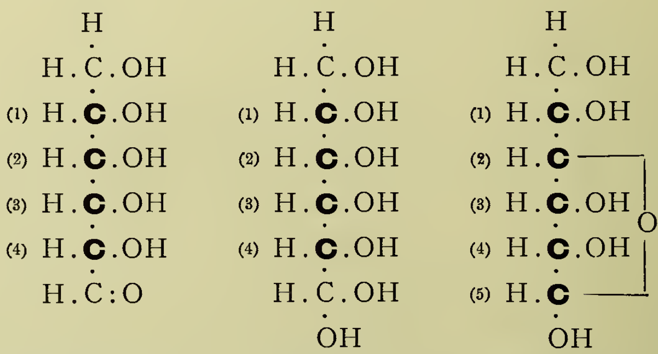
Glucose + $CH_3 \cdot OH$ = Addition compound = H_2O + Methyl-glucoside

It should be noted that whereas glucose contains four asymmetric carbon atoms, the addition compound and the glucoside contain five. From glucose, then, with a definite configuration of the asymmetric carbon atoms (1), (2), (3), and (4), we may obtain two methyl-glucosides, one with the dextro-configuration of the asymmetric atom (5) and one with the lævo-configuration. Two such glucosides are actually known, and are named α- and β-methyl-glucosides. The possibility of similar isomerism of course exists in all glucosides, but only a few have been investigated in this respect.

Mutarotation and Tautomerism of Glucose.

It has already been stated that a freshly prepared solution of glucose shows an optical activity about twice as great as that of the same solution which has stood for some time. Since on crystallisation of the solution with the smaller rotation a solid is obtained which has all the properties of the original solid, and again shows the larger rotation when dissolved afresh, it is evident that some reversible change in constitution must occur in the solution and during the crystallisation. The generally accepted explanation of the phenomenon is the following:—Since glucose is capable of taking up a molecule of methyl alcohol, and subsequently eliminating a molecule of water with formation of a ring anhydride (glucoside), so we may conceive it as taking

up a molecule of water to form an aldehydrol, from which elimination of water with formation of a ring anhydride will produce a substance isomeric with the original glucose. Thus we have:—



Aldehyde formula of glucose — Hypothetical Aldehydrol — Anhydride formula of glucose

The anhydride is here, as it were, a glucoside of water, and contains five asymmetric carbon atoms, so that it must exist in an α and in a β form. If this transformation takes place, we may have in an aqueous solution of glucose, at one and the same time, three isomeric substances capable of reciprocal transformation, namely—the aldehyde, the α-glucoside, and the β-glucoside. In the solution which has been kept till the rotation is constant, glucose exists in the three forms, in equilibrium with each other. These mutually transformable isomers are said to be **tautomeric** forms of glucose. If one of them is partially removed from the equilibrium solution, say the aldehyde form, by means of phenyl-hydrazine, a transformation will take place so as to re-establish the original equilibrium proportions. The whole dissolved substance may then behave as aldehyde, since, as every portion of aldehyde is removed, the conditions for the equilibrium restore it, in part at least, by transformation of the other tautomeric form.

Tautomerism of this kind is of frequent occurrence in organic chemistry, and will be met with occasionally in the sequel.

d-**Fructose**, $C_6H_{12}O_6$.

This ketohexose, which is also known as fruit-sugar or lævulose, is, as the latter name suggests, lævo-rotatory. The symbol *d*- is applied, not to indicate the actual sense of rotation of the substance, but rather a particular configuration of the asymmetric carbon atoms present in the molecule, in this case the correspondence with *d*-glucose. Fructose is found associated with glucose in ripe fruits and in honey, and is formed along with glucose by the inversion of cane-sugar. It is difficult to obtain in the crystalline form. Its calcium compound is somewhat sparingly soluble in water, and affords a means of separating it from glucose, which yields a soluble calcium compound (p. 194). *d*-Fructose, like *d*-glucose, is fermentable by yeast. When treated with phenyl-hydrazine it yields a hydrazone, and subsequently an osazone.

$$\begin{array}{cccc} \mathrm{C:O} & \mathrm{C:N.NHC_6H_5} & \mathrm{C:N.NHC_6H_5} & \mathrm{C:N.NHC_6H_5} \\ \mathrm{H.\dot{C}.OH} & \mathrm{H.\dot{C}.OH} & \mathrm{H.\dot{C}:O} & \mathrm{H.\dot{C}:N.NHC_6H_5} \\ \dot{\mathrm{H}} & \dot{\mathrm{H}} & & \end{array}$$

This osazone is identical in all respects with that obtained from *d*-glucose, so that we may say that the configuration of the asymmetric carbon atoms in *d*-fructose is the same as that of the first three asymmetric carbon atoms of *d*-glucose.

When an osazone is heated with hydrochloric acid solution it is hydrolysed, with reproduction of phenyl-hydrazine, as follows:—

$$\underset{\text{Osazone}}{\begin{array}{c} \mathrm{C:N.NHC_6H_5} \\ \mathrm{H.\dot{C}:N.NHC_6H_5} \end{array}} + \begin{array}{c} \mathrm{H_2O} \\ \mathrm{H_2O} \end{array} = \underset{\text{Osone}}{\begin{array}{c} \mathrm{C:O} \\ \mathrm{H.\dot{C}:O} \end{array}} + \begin{array}{c} \mathrm{H_2N.NHC_6H_5} \\ \mathrm{H_2N.NHC_6H_5} \end{array}$$

The ketone-aldehyde thus formed is termed an **osone**. It is an oxidation product of the aldose or ketose, the alcohol group having been converted into a carbonyl group.

When the osazone derived from *d*-glucose or *d*-fructose is reduced by means of nascent hydrogen, only the aldehyde group is affected and *d*-fructose results. We may consequently convert *d*-glucose into *d*-fructose (or any aldose into the

corresponding ketose) by way of the osazone and osone, with subsequent reduction—

$$
\begin{array}{ccccc}
\mathrm{H.C.OH} & & \mathrm{C{:}O} & & \mathrm{C{:}O} \\
\cdot & & \cdot & & \cdot \\
\mathrm{H.C{:}O} & \longrightarrow & \mathrm{H.C{:}O} & \longrightarrow & \mathrm{H.C.OH} \\
 & & & & \cdot \\
 & & & & \mathrm{H} \\
\text{Aldose} & & \text{Aldosone} = \text{Ketosone} & & \text{Ketose}
\end{array}
$$

d-**Galactose**, $C_6H_{12}O_6$.

This aldohexose may be prepared by hydrolysing milk-sugar and certain vegetable gums by means of dilute acid. It is much less soluble than glucose, and crystallises from water in needles which melt at 168°. It is dextro-rotatory, is capable of slow direct fermentation by yeast, and like *d*-glucose shows the phenomenon of multi-rotation. It can be shown to be an aldose by its oxidation to the corresponding monobasic acid *d*-galactonic acid, $C_6H_{12}O_7$, isomeric with *d*-gluconic acid.

Fermentation and Assimilation of Hexoses.

The four simple sugars: *d*-glucose, *d*-fructose, *d*-galactose, and another, *d*-mannose, have the same configuration of the carbon atoms (1) (2) and (3). These sugars alone are fermentable by yeasts. If, therefore, for example, we add yeast to a racemic mixture of *d*-glucose and *l*-glucose, the former is completely converted into ethyl alcohol and carbon dioxide, whilst the latter is entirely unaffected. Similarly, the same four simple sugars and no others are assimilable by the higher animals. There is frequently this close relation displayed between configuration and the action of enzymes, for it must be borne in mind that decompositions in the animal and vegetable body are generally effected by enzymatic action, and that enzymes are generally specific in their activity.

The action of yeast-juice on *d*-glucose is much less direct than was at first imagined. The first stage of the fermentation is apparently the production of an acid hexose-phosphate, $C_6H_{10}O_4(PO_4H_2)_2$, analogous to glycero-phosphoric acid. This is further attacked and broken up into the products of fermentation with liberation of phosphoric acid, which serves to convert a fresh quantity of glucose into hexose-phosphate.

PENTOSES.

The pentoses contain five oxidised carbon atoms, and may be either aldoses or ketoses. Three are of interest as occurring in plants and animals.

Arabinose, $C_5H_{10}O_5$, is an aldose which may be prepared by hydrolysing gum-arabic with dilute acid. This variety is dextro-rotatory. Its constitutional formula is—

$$CH_2OH \, . \, \mathbf{C}HOH \, . \, \mathbf{C}HOH \, . \, \mathbf{C}HOH \, . \, CO \, . \, H.$$

The racemic modification is present in the urine of patients suffering from pentosuria. As it reduces Fehling's solution, care must be taken to discriminate between it and the glucose produced in diabetes. This may be done by distilling the solution with concentrated hydrochloric acid. A volatile substance, furfuraldehyde (p. 272), is produced from the pentose, and may be detected in the distillate by the addition of a little aniline acetate, with which it gives a red coloration—

$$\underset{\text{Pentose}}{C_5H_{10}O_5} = \underset{\text{Furfuraldehyde}}{C_4H_3O \, . \, CO \, . \, H} + 3H_2O.$$

Hexoses do not give this test.

Xylose, $C_5H_{10}O_5$, is also an aldose, and may be obtained by the hydrolysis of the polysaccharides in plant-cells which have been converted into wood, *e.g.*, from wood, bran, straw. It has been detected in small quantity in the animal body.

Rhamnose, $C_6H_{12}O_5$, is a sugar obtained by the hydrolysis of some glucosides. It is a methyl-pentose and is formulated thus—

$$CH_3 \, . \, \mathbf{C}HOH \, . \, \mathbf{C}HOH \, . \, \mathbf{C}HOH \, . \, \mathbf{C}HOH \, . \, CO \, . \, H.$$

DISACCHARIDES.

The disaccharoses derived from the hexoses have the formula, $C_{12}H_{22}O_{11}$.

Maltose, $C_{12}H_{22}O_{11}$.

Maltose is formed by the action of diastase on starch, and is therefore the chief sugar contained in malt. It crystallises

from water, in which it is very soluble, as small needles which have the composition $C_{12}H_{22}O_{11},H_2O$. Its solutions are dextro-rotatory, and yield *d*-glucose alone on hydrolysis with acid—

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose}}{2C_6H_{12}O_6}.$$

Maltose yields **maltosazone** with phenyl-hydrazine, which may be distinguished from glucosazone by its solubility in boiling water. This osazone has the formula, $C_{12}H_{20}O_9(N:NHC_6H_5)_2$, which indicates that only one of the two characteristic sugar groups, CHOH . CO . H, of the two molecules of glucose, is present in maltose. Maltose readily reduces Fehling's solution. These reactions may be accounted for by the formula—

CH_2OH . CHOH . CH . CHOH . CHOH . CH
|———— O ————|
I. *d*-Glucose residue O
|
CH_2 . CHOH . CHOH . CHOH . CHOH . CO . H
II. *d*-Glucose residue

Here one of the glucose molecules (I.) is represented as forming a glucoside with the other glucose molecule (II.), which retains the characteristic sugar group unaltered, and is thus capable of reducing, forming an osazone, etc. Maltose is readily fermentable by yeast, but only after hydrolysis by maltase contained in the yeast.

Lactose, $C_{12}H_{22}O_{11}$.

This substance is commonly known as milk-sugar, and is contained to the extent of about 5 per cent. in cow's milk, and 6 per cent. in human milk. It may be prepared by evaporating whey — that is, milk from which the fat and proteins have been removed by separation of the cream and curd. The lactose crystallises out and is purified by recrystallisation from water. It is much less soluble in water than the other disaccharoses, 100 parts of the solvent only dissolving 17 parts of lactose at the ordinary temperature, though supersaturated solutions may be easily formed. It crystallises from solution in hard, gritty, well-defined crystals. Its solutions are only

faintly sweet. Lactose reduces Fehling's solution, and forms with phenyl-hydrazine **lactosazone,** which has the same composition as maltosazone, and, like it, is soluble in boiling water, but may be distinguished by its crystalline form.

On hydrolysis with acids or with the enzyme lactase, which occurs in the animal body, it yields *d*-glucose and *d*-galactose—

$$C_{12}H_{22}O_{11} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Galactose}}{C_6H_{12}O_6}.$$

Its constitution may be represented similarly to that of maltose, the galactose being supposed to form a galactoside (analogous to a glucoside) with the glucose molecule, which retains its aldose properties—

$$CH_2OH.CHOH.\underbrace{CH.CHOH.CHOH.CH}_{O}$$

Galactose residue

$$O$$

$$CH_2.CHOH.CHOH.CHOH.CHOH.CO.H$$

Glucose residue

Lactose is only fermentable by yeast after hydrolysis.

Sucrose, $C_{12}H_{22}O_{11}$.

Sucrose, known commonly as cane-sugar, is prepared from the juice of the sugar-cane, or the sugar-beet, which contain respectively about 20 and 17 per cent. of sucrose. It is also obtained in small quantity from the sugar-maple and other plants.

The crushed cane or sliced beet is extracted with water heated to 80° to 90°. The sucrose is originally contained in the cell-liquid, and cannot pass outward through the semi-permeable cell-membrane so long as this remains intact. The high temperature, however, kills the protoplasm and ruptures the cell-membrane, so that the sugar can diffuse into the water with which the plant is surrounded. The extraction is carried out systematically on the counter-current principle, fresh water coming into contact with nearly exhausted material, and

the comparatively concentrated solution meeting fresh material. In this way a sucrose solution of 15 to 20 per cent. may be obtained, but this is contaminated with albuminous substances and with acids and salts present in the sap. Excess of slaked lime is added to neutralise and partly precipitate the acids and to coagulate the proteins. Since calcium hydroxide forms a soluble sucrate with sucrose (p. 205), it is necessary to decompose this by a current of carbon dioxide, which is made to precipitate most of the excess of lime as calcium carbonate. The mixed precipitate is now filtered off by means of a filter-press, and the slightly alkaline filtrate is concentrated by boiling under diminished pressure in vacuum pans. The object of the evaporation under diminished pressure is to keep the temperature as low as possible, so as to avoid hydrolysis of the sucrose. The remainder of the lime is then precipitated as carbonate by means of carbon dioxide. The thick syrup is filtered and further concentrated in vacuum pans to the crystallising-point. On cooling, crystals separate, and are freed from the syrup by means of a centrifugal machine. Further concentration of the syrup and centrifugalisation yields a second quantity of sugar crystals. The sugar so obtained is brown, owing to the small quantity of syrup (molasses) with which it is still mixed. It is refined by dissolving it in hot water, decolorising the solution with animal charcoal, concentrating, and crystallising. About 70 per cent. of the sugar at present manufactured is obtained from the sugar-beet, which can be grown in temperate climates, in contradistinction to the sugar-cane, which can only be cultivated in tropical or subtropical countries.

Sucrose crystallises from water in hard transparent prisms, which melt at 160°. It is very soluble in water, the saturated solution at the ordinary temperature containing 66 per cent., and at 50°, 83 per cent., of sugar. It is practically insoluble in absolute alcohol. If sugar is melted by heating with a very little water, the mass solidifies on cooling to a vitreous amorphous mass, which slowly becomes crystalline (barley-sugar). Between its melting-point and 200°, sugar loses water and turns brown with formation of **caramel**, or burnt-sugar, which is a mixture of various substances, and is used as a flavouring and colouring material.

Sucrose readily forms sucrates with the alkalies and

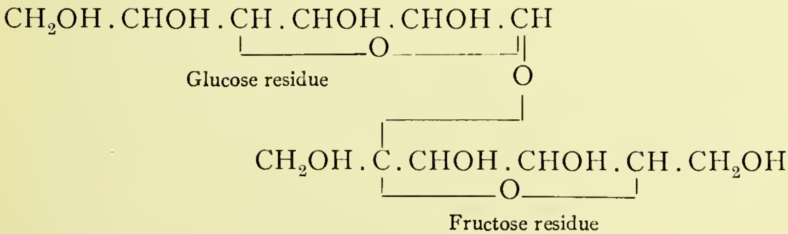
alkaline earths. Owing to the solubility of the compound $C_{12}H_{21}O_{11}.Ca.OH$, calcium hydroxide dissolves more readily in cane-sugar solution than in water, and advantage is taken of this fact in the preparation of the *liquor calcis saccharatus* of the Pharmacopœia, which contains about ten times as much lime as lime-water.

As has already been explained, sucrose on hydrolysis by acids or enzymes yields *d*-glucose and *d*-fructose—

$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Fructose}}{C_6H_{12}O_6},$$

the original dextro-rotation of the sucrose being inverted or changed to a lævo-rotation in the process. The hydrolysis with acid takes place much more readily than is the case with maltose and lactose.

Sucrose does not yield a specific osazone with phenyl-hydrazine, nor does it reduce Fehling's solution. The absence of these reactions, which distinguish it from the other sugars, would indicate that there is, properly speaking, no sugar group —CHOH.CO— in sucrose at all. This behaviour may be accounted for by the following formula:—



The carboxyl groups of both hexoses are here represented as being involved in the union of the two molecules, which are therefore both in the glucosidic condition, with consequent disappearance of the characteristic properties of the true sugars.

Sucrose is not directly fermentable by yeast, but since yeast always contains an enzyme, invertase, which hydrolyses the sucrose with production of the fermentable hexoses, the fermentation can be carried out practically without difficulty. Similarly, owing to inversion sucrose yields glucosazone on prolonged heating with phenyl-hydrazine.

TRISACCHARIDES.

The only well-known trisaccharide is **raffinose**, $C_{18}H_{32}O_{16}$, found in Australian manna and in the molasses from beet-sugar. Like cane-sugar, it has no action on phenyl-hydrazine or on Fehling's solution, so that it contains no true sugar group. On complete hydrolysis by means of dilute acid it decomposes as follows :—

$$\underset{\text{Raffinose}}{C_{18}H_{32}O_{16}} + 2H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Fructose}}{C_6H_{12}O_6} + \underset{\text{Galactose}}{C_6H_{12}O_6}.$$

POLYSACCHARIDES.

We have already seen that important polysaccharides of the empirical formula, $C_6H_{10}O_5$, are to be found in dextrin, starch, and cellulose. With regard to the molecular weight of these compounds little can be said. It is generally assumed to be very high. This conclusion is based on the fact that very low values of osmotic pressure, depression of freezing-point, etc., are observed with their solutions. It must be remembered, however, that the solutions are colloidal, and it is not known how far we can rely on the experimental methods just mentioned to give true molecular weights for colloid solutions.

Even if the very large molecular weight given by the osmotic pressure or allied methods are accurate, these molecular weights are the molecular weights of aggregates of associated molecules, and it is not those but the minimum molecular weights, *i.e.* the weight of the simple unassociated and undecomposed molecule, that is of importance from the point of view of organic chemistry. Thus if we determine the molecular weight of acetic acid in benzene solution by the freezing-point method, we find that it is approximately 120, *i.e.* that it corresponds to the formula, $C_4H_8O_4$, but the value yielded by the vapour density or by the freezing-point of an aqueous solution is only 60, and corresponds to the simple formula, $C_2H_4O_2$. It is this latter minimum value that is of systematic interest, *i.e.* of interest from the point of view of formulation, and we never write the formula otherwise than $C_2H_4O_2$.

If we dissolve "soluble starch" in formamide instead of in

water, and determine the molecular weight by the freezing-point method, we find it to be 645. This corresponds to the formula $(C_6H_{10}O_5)_4$, which is the minimum formula for starch at present known. Against this formula it might be urged that by its means an adequate representation cannot be given of all the intermediate stages between starch and maltose which are produced when an aqueous solution of starch is decomposed by the aid of diastase. Since, however, we are without knowledge of the minimum molecular weight of the dextrins, which have not yet been investigated in true solution in any solvent, the question of the molecular complexity of starch may still be regarded as open.

Inulin, $(C_6H_{10}O_5)_n$, is found instead of starch as reserve material in some compositæ, and may be obtained most conveniently from dahlia bulbs. It is a white powder which dissolves easily in warm water. On being heated alone it forms products resembling dextrin, and on hydrolysis by means of dilute acid it yields *d*-fructose. It is not coloured by iodine, and diastase is practically without action on it.

Glycogen, $(C_6H_{10}O_5)_n$, is the analogue of starch in the animal organism. It is found to the extent of about 0·6 per cent. in muscle, and in large quantity in the liver, especially after a meal of carbohydrates. It is formed in the liver from the *d*-glucose which passes into the blood from the alimentary canal, is stored there, and reconverted by enzymes into *d*-glucose as required. It is a white amorphous powder which readily gives an opalescent solution with warm water. It yields a red or brown coloration with iodine, and is converted by diastatic ferments and by dilute acids into the same substances as are obtained from starch.

Natural gums are sometimes classed with the polysaccharides, because on hydrolysis with acids they yield simple hexoses and pentoses (*e.g.* arabinose from gum-arabic). They, contain in the complex molecule, however, acid residues in addition to the simple sugar residues, these acid residues being mostly in the form of alkaline and alkaline earth salts. They swell up or dissolve in water, yielding gummy or mucilaginous solutions.

Cellulose and its Derivatives.

Cellulose, $(C_6H_{10}O_5)_n$, is the most complex of the polysaccharides, but is not to be regarded as a polymerised form of starch, inasmuch as the disaccharide obtained from it by hydrolysis is totally different from the maltose obtained from starch. It is an essential constituent of the cell-wall of plants, and is familiar in a state approaching purity in the form of cotton-wool and filter-paper. It is the basis of the cotton and paper industries. We are altogether without information as to its molecular weight, as it can neither be volatilised nor dissolved unchanged in any solvent. When treated with ammoniacal cupric hydroxide (Schweitzer's reagent) it passes into colloidal solution, and may be reprecipitated by acids as a white coagulum.

Cellulose is acted on by acids with formation of esters. Each unit $C_6H_{10}O_5$ contains three hydroxyl groups, so that we may write the formula, $C_6H_7O_2(OH)_3$. These three alcoholic hydroxyl groups may be converted by the action of acids into ester residues. Thus, nitric acid may yield mono-, di-, or trinitrate, $C_6H_7O_2(OH)_2(ONO_2)$, $C_6H_7O_2(OH)(ONO_2)_2$, or $C_6H_7O_2(ONO_2)_3$, according to the conditions of the action. If cellulose in the form of filter-paper is dipped for a few minutes into concentrated sulphuric acid, it is superficially converted into an acid disulphate, thus—

$$C_6H_7O_2(OH)_3 + 2H_2SO_4 \rightleftharpoons C_6H_7O_2(OH)(SO_4H)_2 + 2H_2O.$$

This substance is decomposed by the action of water, with regeneration of cellulose, so that when the treated filter-paper is washed in water the cellulose is deposited on the surface and in the pores of the paper, which is now much tougher than the original, and is known as parchment paper or **vegetable parchment**. It is extensively used as a membrane for dialysis.

Pyroxylin and Gun-cotton.—When cellulose, usually in the form of purified cotton waste, is soaked in a mixture of one part concentrated nitric acid and three parts concentrated sulphuric acid for twenty-four hours at a low temperature, it is converted into the trinitrate $C_6H_7O_2(NO_3)_3$. This substance is then washed absolutely free from acid, and dried. It retains

the original fibrous structure of the cotton, from which, however, it may be distinguished by its being crisper and harsher to the touch. When loose and unconfined it burns rapidly with a large flame. When compressed it explodes violently on detonation. It is used as an explosive by itself as gun-cotton, and also in conjunction with nitroglycerine in cordite and other military explosives (smokeless powders). For the combustion of the carbon and hydrogen in the trinitrate to carbon monoxide and water 9·5 atoms of oxygen are required, as against eleven actually contained in the compound, so that there is a sufficient supply of nitrate oxygen for complete conversion into gaseous products.

Gun-cotton is insoluble in water, alcohol, and ether, and in a mixture of the last two solvents.

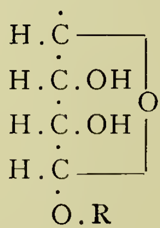
If the cotton is nitrated with a mixture of the concentrated acids diluted with about 10 per cent. of water, a product is obtained which is essentially the dinitrate, $C_6H_7O_2(OH)(NO_3)_2$. This substance, often known as **pyroxylin** or **collodion**, is soluble in a mixture of alcohol and ether, and likewise in ethyl acetate and in acetone. Its explosive effect is much less than that of gun-cotton. When a thin layer of the solution in ether-alcohol or ethyl acetate is allowed to evaporate, the collodion is left in the form of a transparent continuous film. Such films are used in surgery ("new skin," etc.) and in photography. A purified form of pyroxylin is used under the name of **celloidin** for similar purposes, and for imbedding microscopic preparations.

When pyroxylin is incorporated with camphor by the aid of a small quantity of alcohol, it forms a dough-like mass which when pressed and dried yields the tough elastic material known as **celluloid**. Celluloid though inflammable is not explosive. It may be easily cut and turned, and can also be moulded if heated to about 80°, at which temperature it is soft and plastic. With the necessary pigments and fillers it may be used to produce imitations of ivory, tortoise-shell, amber, etc.

Acetates and formates of cellulose.—These esters are now produced as substitutes for the nitrates (collodion) in the manufacture of cinematograph films, etc. They are much less inflammable than the corresponding nitrates, whilst possessing similar physical properties.

NATURAL GLUCOSIDES.

The glucosides found in nature are of similar structure to methyl-glucoside, being formed from a simple sugar and another molecule with elimination of water. The general formula is—



They may be hydrolysed by dilute acids or by enzymes, with production of a sugar and the substance with which the sugar was combined. The sugar is for the most part *d*-glucose, but other pentoses and hexoses (*e.g.* rhamnose and fructose) are occasionally found. The other constituent of the glucoside molecule is very variable, phenols, aromatic alcohols, aldehydes, and esters being of common occurrence.

The pharmacologically active principles in many plants are glucosides, *e.g.*, those of digitalis, strophanthus, bitter almonds. Along with glucosides in plants are found the enzymes which are capable of rapidly hydrolysing them, but since glucoside and enzyme do not occur in the same cell, there is normally no action of hydrolysis. The hydrolysis by means of dilute acid requires a very considerable time even at the boiling-point.

A few simple glucosides are described below.

Arbutin, $C_{12}H_{16}O_7$, is obtained from the leaves of the bear-berry (*Arbutus uva ursa*). When hydrolysed by acid or by the enzyme **emulsin**, obtained from sweet almonds, it yields glucose and quinol, thus—

$$\underset{\text{Arbutin}}{C_{12}H_{16}O_7} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Quinol}}{m\text{-}C_6H_4(OH)_2}.$$

Its formula may be written—

$$CH_2OH.CHOH.\underbrace{CH.CHOH.CHOH.CH}_{O}.O.C_6H_4(OH).$$

It occurs in colourless crystals, which possess a bitter taste, and have powerful antiseptic properties, on which account the glucoside is sometimes used in medicine.

Salicin, $C_{13}H_{18}O_7$, is the active principle in willow bark, and is used in the treatment of rheumatism, malarial fever, etc. It yields glucose and salicylic alcohol (saligenin) on hydrolysis by emulsin or by acids, thus—

$$\underset{\text{Salicin}}{C_6H_{11}O_5 . O . C_6H_4 . CH_2OH} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Saligenin}}{HO . C_6H_4 . CH_2OH.}$$

Like arbutin, it is a bitter crystalline solid, with antiseptic properties.

Amygdalin, $C_{20}H_{27}O_{11}N$, is the active principle of bitter almonds, and was one of the earliest glucosides to be studied. It is a slightly bitter crystalline solid, soluble in about twelve parts of water. On hydrolysis by emulsin or dilute acids it decomposes as follows :—

$$\underset{\text{Amygdalin}}{C_{20}H_{27}O_{11}N} + 2H_2O = \underset{\text{Glucose}}{2C_6H_{12}O_6} + \underset{\text{Benzaldehyde}}{C_6H_5 . CO . H} + \underset{\text{Hydrocyanic acid}}{HCN.}$$

Its formula is probably $C_6H_{11}O_5 . O . C_6H_{10}O_4 . O . CH(CN) . C_6H_5$.

It will be observed that the hydrocyanic acid in the original molecule is bound to the benzaldehyde, which readily forms an addition compound with it—

$$\underset{\text{Benzaldehyde}}{C_6H_5 . \overset{\displaystyle O}{C} . H} + \underset{\text{Hydrocyanic acid}}{HCN} = \underset{\text{Mandelic nitrile}}{C_6H_5 . \overset{\displaystyle H}{\overset{\displaystyle O}{C}} . H \atop \quad CN}$$

This mandelic nitrile may be conceived to have formed a glucoside with a disaccharide which on hydrolysis yields two molecules of glucose.

Many glucosides besides amygdalin yield hydrocyanic acid on hydrolysis, *e.g.*, *vicianin*, from a wild vetch, *linamarin*, from young flax plants, *prulaurasin*, from the cherry laurel.

Sinigrin, $C_{10}H_{16}O_9NS_2K$, is an example of a mustard-oil

glucoside. It is found in the seeds of black mustard, and on hydrolysis it breaks up as follows :—

$$\underset{\text{Sinigrin}}{C_{10}H_{16}O_9NS_2K} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Allyl isothiocyanate}}{C_3H_5.NCS} + KHSO_4.$$

The seeds contain the enzyme myrosin, which is capable of effecting the hydrolysis : emulsin in this case has no action.

When the seeds, which if quite dry are practically inodorous, are crushed with a little water, the glucoside and the enzyme are brought into contact, and the pungent odour of allyl isothiocyanate is at once recognisable. The volatile oil of mustard of the Pharmacopœia prepared by the distillation from black mustard seeds after maceration with water contains allyl isothiocyanate. Ordinary mustard is a mixture of the seeds of white and of black mustard. The former contains the glucoside **sinalbin**, which also hydrolyses with formation of a volatile isothiocyanate.

Indican, $C_{14}H_{17}O_6N$, is a vegetable glucoside which must be distinguished from urinary indican, a related substance of different chemical character. It occurs in plants which yield indigo, and on hydrolysis it is decomposed into glucose and indoxyl—

$$\underset{\text{Indican}}{C_{14}H_{17}O_6N} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Indoxyl}}{C_8H_7ON}.$$

Indican may be hydrolysed by emulsin, but only slowly. The enzyme present in the leaves of the plant, indimulsin, hydrolyses it much more rapidly. Indoxyl is a colourless substance, but readily oxidises to the blue colouring matter indigotin under the influence of an oxydase, also contained in the plant.

HYDRO-AROMATIC SUBSTANCES.

Some aromatic substances, when reduced, take up hydrogen in the benzene ring and become what we term hydro-aromatic substances. These compounds do not in general possess the reaction of aromatic substances proper, but must from their behaviour be regarded as cyclic compounds of the fatty series.

Hexahydrobenzene, or *cyclohexane*, C_6H_{12}.—When benzene

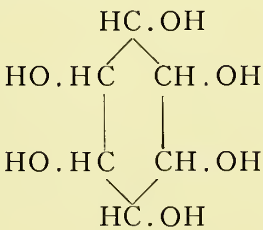
vapour mixed with hydrogen is passed over finely divided nickel, which acts as a catalyst, the two substances unite to produce hexahydrobenzene—

$$C_6H_6 + 3H_2 = C_6H_{12}.$$

It is a colourless liquid boiling at 81°, and occurs, together with its homologues, in Russian petroleum (p. 102). With nitric acid it yields no nitro product as in the case of benzene, but is oxidised to adipic acid—

$$\begin{array}{l} CH_2.CH_2.CH_2 \\ \vdots \qquad\quad\;\, \vdots \\ CH_2.CH_2.CH_2 \end{array} + 5(O) = \begin{array}{l} CH_2.CH_2.COOH \\ \vdots \\ CH_2.CH_2.COOH \end{array} + H_2O.$$

Inositol, *hexahydroxy-cyclohexane*, $C_6H_{12}O_6$.—The graphic formula of this substance is—



Inositol

It has the empirical formula $C_6H_{12}O_6$, which is identical with that of the simple hexoses. Since, in addition, it possesses like these a sweet taste, it was formerly looked upon as a sugar and was spoken of as an aromatic or cyclic sugar. It displays, however, none of the reactions of a sugar proper; and, as we have seen, a sweet taste is frequently possessed by polyhydric alcohols. It occurs in small quantity in practically all animal tissues, and is also found in plants. This natural variety is optically inactive and incapable of resolution into active components. Optically active inositols, however, also occur in plants, so that on the whole we know, as in the case of tartaric acid, two optically active modifications, one dextro- and the other lævo-rotatory, the optically inactive modification by internal compensation, and an inactive racemic mixture of the two active varieties. Since the formula possesses no asymmetric carbon atom, the optical activity must be due to the asymmetry of the

molecule as a whole. In recent years other examples have been obtained of optically active asymmetric molecules which possess no asymmetric atoms in their structure.

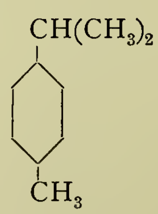
Inositol is freely soluble in water, and in general possesses the properties of a polyhydric alcohol. It does not reduce Fehling's solution.

TERPENES.

When shallow cuts are made in the stem of coniferous trees a liquid gradually oozes from these cuts which is known by the name of **turpentine.** Turpentine may also be produced by the destructive distillation of coniferous woods, care being taken that the temperature to begin with should not be too high and that the heat should be uniformly distributed. Wood spirit, wood tar, and charcoal are the other products of the distillation.

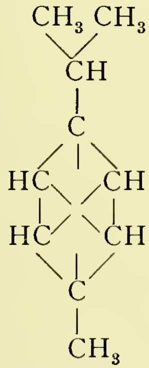
Crude turpentine when subjected to distillation with steam, separates into an oil which passes over and condenses with steam, and a solid non-volatile resin which remains behind. The oil which comes over with the steam is known as **oil of turpentine.** It boils at about 160°, has a specific gravity of 0.85, and is insoluble in water. When exposed to air it gradually becomes more viscous, and hardens, being slowly converted into resinous substances. It is largely used in the preparation of varnishes, owing to this property of drying and hardening on exposure to air.

Oil of turpentine consists principally of a hydrocarbon named **pinene,** $C_{10}H_{16}$. This substance is a representative of the group of terpenes, which occur abundantly in the volatile oils from many plants. The terpenes proper, or monoterpenes, have the formula $C_{10}H_{16}$. They behave as unsaturated hydrocarbons, and many of them are related to the hydrocarbon **cymene,** or *p*-methyl-isopropyl-benzene—

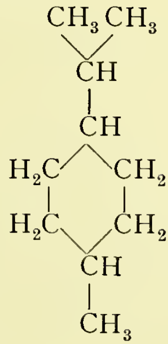


which has the composition $C_{10}H_{14}$.

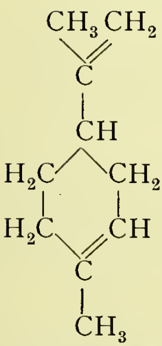
Notwithstanding their identity of composition, the terpenes differ very much from each other in constitution, some of them uniting with two atoms of bromine to form compounds $C_{10}H_{16}Br_2$, others uniting with four atoms to form compounds $C_{10}H_{16}Br_4$. The graphic formulæ of the principal terpenes are given together in the following table in order that their relationship to each other may be apparent—



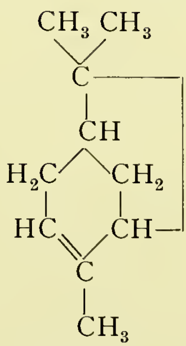
Cymene, $C_{10}H_{14}$,
Aromatic hydrocarbon



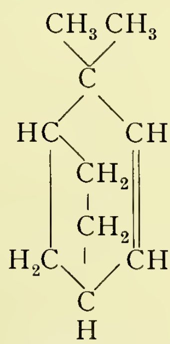
Hexahydro-cymene, $C_{10}H_{20}$
Saturated cyclic hydrocarbon



Limonene, $C_{10}H_{16}$,
one ring,
doubly unsaturated



Pinene, $C_{10}H_{16}$,
two rings,
singly unsaturated



(?)

Camphene, $C_{10}H_{16}$,
two rings,
singly unsaturated

Terpenes

In pinene and camphene the molecule contains two rings instead of the single ring found in limonene. The formation of the extra ring involves the removal of two hydrogen atoms from the carbon atoms which are newly joined, and is thus, so far as composition is concerned, equivalent to a double bond (p. 151).

Pinene, $C_{10}H_{16}$, is an optically active liquid which is the chief constituent of oil of turpentine. It combines readily, not only with bromine, but also with hydrochloric acid, the product of the union being pinene hydrochloride, $C_{10}H_{17}Cl$, which is a white solid with an odour resembling camphor, and is sometimes known as "artificial camphor." Both *d*-pinene and *l*-pinene occur naturally.

Camphene, $C_{10}H_{16}$, is a solid hydrocarbon which melts about 48° and has a smell resembling both turpentine and camphor. It occurs in ginger oil, camphor oil, etc., and is optically active. It likewise combines with hydrochloric acid to form bornyl chloride. Its constitution has not been determined with certainty.

Limonene, $C_{10}H_{16}$, occurs in the essential oil of lemon, lavender, caraway, etc. It is a colourless dextro-rotatory liquid which differs from the two preceding terpenes by uniting with four atoms of bromine, or with two molecules of hydrochloric acid. The lævo-rotatory isomeride also occurs in nature.

The inactive or *dl*- modification of limonene is named **dipentene**, and is formed, not only when limonene is heated to a temperature of about 300°, but also when pinene or camphene are similarly treated. This behaviour shows that, notwithstanding the great apparent difference in constitution between these three important terpenes, the actual relationship between them is close.

These and other terpenes occur, together with esters, etc., in **volatile oils**, the pharmacological action of which is similar to that of oil of turpentine. They are generally employed externally, and have an irritant action on the skin. They usually also possess a slight antiseptic action.

Besides these monoterpenes, or terpenes proper, other substances exist, the formulæ of which are multiples of C_5H_8. They have properties resembling those of the terpenes, and are distinguished as sesquiterpenes, $C_{15}H_{24}$, diterpenes, $C_{20}H_{32}$, etc., according to the relationship which their formula bears to that of the monoterpenes, $C_{10}H_{16}$.

India-rubber is the most important of the polyterpenes, and is prepared from milk juice of several species of plant. It is generally of a brownish black colour as met with in commerce, but the pure hydrocarbon is a colourless amorphous solid. It

is insoluble in water and alcohol, but dissolves in hydrocarbon solvents (p. 155), carbon bisulphide, and chloroform. It acquires remarkable elasticity after taking up sulphur by being warmed with it, and becoming thereby "vulcanised."

When pure rubber is heated, a hydrocarbon, C_5H_8, distils off. This hydrocarbon is known as **isoprene**, and has the following constitution :—

$$\begin{array}{c} CH_2 : \underset{\displaystyle CH_3}{\overset{\cdot}{C}H} . CH : CH_2 \end{array}$$

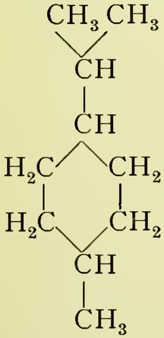
Isoprene

Isoprene is a diolefine, and may be prepared by other methods. When heated for a long time with concentrated hydrochloric acid, or more rapidly with sodium, it produces substances by polymerisation which are apparently identical with pure rubber, or very closely resemble it. The molecular weight of rubber has not been established with certainty.

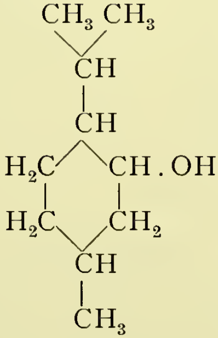
OXYGEN COMPOUNDS RELATED TO THE TERPENES.

Menthol, $C_{10}H_{20}O$.

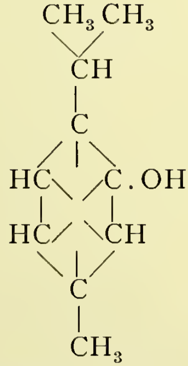
This substance is the chief constituent of oil of peppermint. It is a solid which melts at 42°, and possesses a strong odour of peppermint. Its chemical behaviour shows that it is an alcohol, and it has been proved to have the constitution of hydroxy-hexahydro-cymene—



Hexahydro-cymene, $C_{10}H_{20}$



Menthol, $C_{10}H_{19}.OH$



Thymol, $C_{10}H_{13}.OH$

It is employed in medicine for the most part externally. When

rubbed on the skin it first produces a burning sensation, followed by a sensation of cold. It has antiseptic properties, but, as its formula shows, it is not a phenol. When it is treated by appropriate oxidising agents it loses six atoms of hydrogen, one from each carbon of the ring, and is converted into thymol, a true phenol (p. 164).

Terpin, $C_{10}H_{20}O_2$.

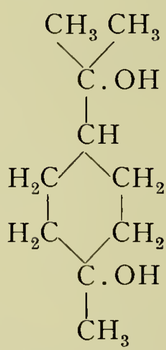
Terpin may be formed by the hydration of pinene or limonene—

$$C_{10}H_{16} + 2H_2O = C_{10}H_{20}O_2.$$

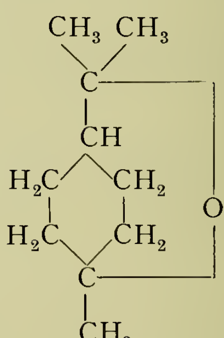
It is a dihydroxy derivative of hexahydro-cymene (see below).

Cineol, $C_{10}H_{18}O$.

Cineol, or **eucalyptol,** may be regarded as an anhydride or internal ether of terpin, to which it bears the same relation as ethylene oxide does to glycol. It is a liquid which smells of camphor, and occurs in oil of eucalyptus. The relationship between its formula and that of terpin is shown below—



Terpin, $C_{10}H_{18}(OH)_2$



Cineol, $C_{10}H_{18}O$

Borneol, $C_{10}H_{18}O$.

This substance, known also as Borneo camphor, occurs in numerous essential oils. It is a solid which has an odour resembling that of camphor, and may be converted into camphor, $C_{10}H_{16}O$, by oxidation. It has the peculiarity that its melting-point, 203°, lies very close to its boiling-point, 212°. Its

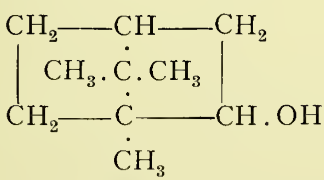
relationship to the terpenes is practically established by the fact that when heated with potassium hydrogen sulphate it loses water and is converted into camphene—

$$\underset{\text{Borneol}}{C_{10}H_{18}O} = \underset{\text{Camphene}}{C_{10}H_{16}} + H_2O.$$

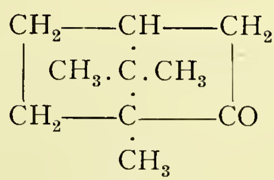
Camphor, $C_{10}H_{16}O$.

This substance is extracted on a large scale from the camphor laurel, which occurs in China and Japan. The wood is boiled with water, and both camphor and camphor-oil pass over and are condensed with the steam. The solid camphor is pressed free from the oil, and is purified by sublimation. It sublimes easily, its melting-point being 175°, and its boiling-point 209°. It is largely used, not only as a medicinal agent, but also in the manufacture of celluloid and explosives. The ordinary camphor is dextro-rotatory. The lævo-rotatory variety occurs in matricaria camphor.

Camphor has all the properties of a ketone, forming, for example, an oxime which melts at 118°. As has been stated, it may be formed from borneol by oxidation. It bears to this substance the relation of a ketone of the corresponding secondary alcohol, as may be seen from the following constitutional formulæ :—



Borneol



Camphor

NITROGENOUS ORGANIC COMPOUNDS.

By the successive removal of the hydrogen atoms from water we obtain the univalent radical hydroxyl —OH, and the bivalent radical =O. Similarly, by the successive removal of the three hydrogen atoms of ammonia we obtain the univalent group $—NH_2$, generally called the **amino** group, the bivalent **imino** group =NH, and the trivalent radical ≡N. The following table shows the relationship of these groups according to their valency :—

	Univalent.	Bivalent.	Trivalent.
Oxygenous .	—OH	=O	$\begin{cases} —OH \\ =O \end{cases}$
Nitrogenous .	$—NH_2$	=NH	≡N

The various groups, oxygenous on the one hand and nitrogenous on the other, not only correspond with regard to their valency, but may frequently be directly substituted one for the other. Thus, in a compound containing the amino group $—NH_2$, it is often possible by the process of hydrolysis to substitute for it the hydroxyl group —OH, with simultaneous formation of ammonia. Conversely, by the action of ammonia on the oxygen compounds we can often substitute the equivalent nitrogenous groups. Many instances of such substitution are afforded by the nitrogenous derivatives of the two single-carbon acids—

$$\underset{\text{Formic acid}}{H.COOH} \quad \text{and} \quad \underset{\text{Carbonic acid}}{HO.CO.OH.}$$

Thus, if all the oxygen radicals in formic acid are replaced by nitrogen, the substances HCN is obtained. This substance, known as hydrocyanic acid or prussic acid, is the acid corresponding to the cyanides, many of which are of great importance.

CYANOGEN DERIVATIVES.

Hydrocyanic acid may be looked upon as consisting of the positive radical, $H^{\cdot}$, and the radical of the cyanides, CN'. The latter radical when no reference is made to its electrical charge is generally known as the cyanogen radical, and plays an important part in organic chemistry.

Cyanides are manufactured by a variety of processes. One of the simplest and most direct methods is that in which nitrogen is led at a high temperature over barium carbide. The two substances react according to the following equation :—

$$\underset{\text{Barium carbide}}{BaC_2} + N_2 = \underset{\text{Barium cyanide}}{Ba(CN)_2}$$

From this substance potassium cyanide may be produced by the action of potassium carbonate in aqueous solution. The action may be represented as follows :—

$$Ba(CN)_2 + K_2CO_3 = BaCO_3 + 2KCN.$$

The barium carbonate is filtered off, and the solution of potassium cyanide, which is very soluble in water, is evaporated to dryness.

The cyanides in solution closely resemble the chlorides in their tests. Thus, silver cyanide is not only insoluble in water, but practically also in nitric acid. A solution of a cyanide may, however, be readily distinguished from that of a chloride by the addition of a soluble salt of zinc, zinc cyanide being insoluble in water, whereas zinc chloride is freely soluble. The cyanides have a great tendency to form double salts with a complex cyanide ion. For example, insoluble silver cyanide dissolves readily in a solution of potassium cyanide, with formation of a new substance of the formula $K^{\cdot}Ag(CN)_2'$, which acts as potassium salt, and is, therefore, soluble in water. Potassium ferrocyanide and potassium ferricyanide, which will be dealt with later, are important double cyanides of this character.

Hydrocyanic Acid, HCN.

This acid may be prepared by distilling a solution of potassium cyanide or of potassium ferrocyanide with dilute sulphuric acid. Hydrocyanic acid is liberated, and being

volatile, passes over with the steam, so that a solution of hydrocyanic acid is obtained. The pure anhydrous acid may be prepared by the fractional distillation of such a solution, the last quantities of water being removed by means of calcium chloride. It is a colourless, very volatile liquid, boiling at 25°. Both the vapour and the solution are extremely poisonous. The dilute acid used in medicine contains only 2 per cent. of the acid.

Hydrocyanic acid is a very feeble acid, its solution scarcely reddening litmus. Its salts are, therefore, more or less hydrolysed in aqueous solution, solutions of potassium and sodium cyanide having a marked alkaline reaction.

Its relationship to formic acid is shown by its decomposition in aqueous solution. When a solution has been kept for some time it is found to contain ammonium formate, which has been apparently produced according to the following equation:—

$$HCN + 2H_2O = H.COONH_4.$$

The reverse reaction may be effected by heating ammonium formate with phosphorus pentoxide, which removes the elements of water from the formate and liberates hydrocyanic acid. The constitution of hydrocyanic acid has not yet been determined with certainty. It may either be—

$$H.C \vdots N \quad \text{or} \quad H.N:C.$$

In the last formula the carbon is represented as a dyad element, as it is in carbon monoxide, C : O. It will be remembered that carbon monoxide is in a sense the anhydride of formic acid, and if we replace in it the dyad oxygen by the dyad radical, NH, then we obtain this second formula for hydrocyanic acid.

It is quite possible that here we have a case of tautomerism, the actual liquid hydrocyanic acid consisting of an equilibrium mixture of two different substances having the above constitutions. Some of the salts of hydrocyanic acid would seem to be derived from one of these and some from the other.

Mercuric cyanide, $Hg(CN)_2$, which may be prepared by dissolving mercuric oxide in hydrocyanic acid, is an exceptional salt, inasmuch as it is practically non-ionised, when dissolved in water. Its aqueous solutions, therefore, are anomalous, both with regard to many of the tests for mercury and many of the tests

for cyanides, since most of the precipitation tests employed are tests for ionised and not for non-ionised substances.

Nitriles and Isonitriles.

That hydrocyanic acid probably exists in two tautomeric forms is supported by the fact that two isomeric sets of esters may be derived from it. These alkyl cyanides are known respectively as **nitriles** and **isonitriles.**

If potassium cyanide is heated with potassium ethyl sulphate, a double decomposition takes place—

$$KCN + KC_2H_5SO_4 = K_2SO_4 + C_2H_5.C \vdots N.$$

The **ethyl cyanide** formed in this way is a liquid which boils at 97°, and on reduction with nascent hydrogen yields the base propylamine—

$$\underset{\text{Ethyl cyanide}}{CH_3.CH_2.C \vdots N} + 4(H) = \underset{\text{Propylamine}}{CH_3.CH_2.CH_2.NH_2}.$$

The formation of this substance on reduction clearly indicates that the carbon of the cyanogen radical is attached to the carbon of the ethyl group.

Ethyl cyanide, unlike ethyl chloride, is freely soluble in water, and possesses a characteristic, not unpleasant odour.

When its solution is boiled with dilute acids it is hydrolysed with formation of propionic acid—

$$C_2H_5.CN + 2H_2O + HCl = C_2H_5.COOH + NH_4Cl.$$

In this process of hydrolysis the triad nitrogen atom is replaced by the dyad oxygen and the monad hydroxyl, and thus the cyanogen group is converted into the characteristic carboxyl group of the acids. In accordance with this clear relationship to the acids, these and similar cyanides are called acid nitriles. Ethyl cyanide is, therefore, frequently referred to as **propionitrile,** and methyl cyanide, $CH_3.CN$, is similarly termed **acetonitrile** because it may be readily hydrolysed with formation of acetic acid.

Isomeric with these nitriles are the **isonitriles** or **carbylamines**, which may be formed by the action of alkyl iodides on

silver cyanide. For example, when ethyl iodide is heated with silver cyanide the following reaction takes place:—

$$AgCN + C_2H_5I = AgI + C_2H_5.NC.$$

The liquid so produced boils 20° lower than ethyl cyanide (propionitrile), is sparingly soluble in water, and possesses a penetrating, offensive odour. When boiled with dilute acids it does not hydrolyse with formation of propionic acid and ammonia, but with production of formic acid and ethylamine—

$$C_2H_5.NC + 2H_2O = C_2H_5.NH_2 + H.COOH.$$

This behaviour would indicate that in it the ethyl group is united, not to the carbon of the cyanogen radical as in propionitrile, but to the nitrogen of the cyanogen radical. We therefore write the formula of ethyl isonitrile as $C_2H_5.N:C$.

Complex Metallic Cyanides.

We have already seen that silver cyanide dissolves in potassium cyanide to form the complex salt potassium argentocyanide $K^{\cdot}Ag(CN)_2'$. The cyanides of many other metals are similarly affected by solutions of the alkaline cyanides. The most important complex cyanides are those derived from iron.

Potassium ferrocyanide, $K_4{}^{\cdot}Fe(CN)_6''''$.—This salt is prepared on a large scale by fusing together potassium carbonate, iron filings, and nitrogenous animal matter, such as horn shavings, hoof-parings, hair, and the like. After cooling, the mass is extracted with water and the solution filtered. On evaporation, potassium ferrocyanide crystallises in the form of a trihydrate. This hydrate is of a bright yellow colour, and is commonly known as yellow prussiate of potash. With ferric salts it yields a deep blue precipitate of **Prussian blue.** When boiled with dilute sulphuric acid it yields hydrocyanic acid, but when warmed with concentrated sulphuric acid, the cyanide is hydrolysed with evolution of carbon monoxide (compare p. 222).

Potassium ferricyanide, $K_3{}^{\cdot}Fe(CN)_6'''$.—This substance is prepared by oxidising potassium ferrocyanide. The oxidation is usually effected in solution by means of chlorine—

$$2K_4{}^{\cdot}Fe(CN)_6'''' + Cl_2 = 2K^{\cdot}Cl' + 2K_3{}^{\cdot}Fe(CN)_6'''.$$

Potassium ferricyanide separates in the form of deep red crystals which yield a yellow solution. It is commonly known as red prussiate of potash. With a solution of a ferric salt it produces a dark brown solution, with a ferrous salt a deep blue precipitate which is apparently identical with Prussian blue.

Cyanogen, C_2N_2.

If mercuric cyanide is strongly heated it breaks up into metallic mercury and a gas called cyanogen—

$$Hg(CN)_2 = Hg + C_2N_2$$

This gas, which has the molecular formula C_2N_2, bears the same relation to the cyanide radical as chlorine gas does to the chloride radical. Its constitutional formula is $N\vdots C.C\vdots N$. That the carbon atoms are directly united together, is proved by its hydrolysis. When boiled with dilute acid it is converted into oxalic acid and ammonia, according to the equation—

$$N\vdots C.C\vdots N + 4H_2O = HOOC.COOH + 2NH_3.$$

The ammonia is, of course, not liberated as such, but combines either with the oxalic acid or with the acid used in effecting the hydrolysis. Since, in oxalic acid, the two carbonic atoms are joined together, we may draw the conclusion that in cyanogen gas they are likewise directly united.

Cyanogen is a highly poisonous compound. It is combustible in air, burning with a peach-coloured flame, the products of combustion being carbon dioxide and nitrogen.

When cyanogen is led into a solution of potassium hydroxide it behaves very much as chlorine does under similar circumstances, giving a mixture of potassium cyanide and potassium cyanate instead of chloride and hypochlorite—

$$\begin{array}{llllll} 2KOH + Cl_2 & = & KCl & + KClO & + H_2O \\ 2KOH + (CN)_2 & = & \underset{\text{Cyanide}}{KCN} & + \underset{\text{Cyanate}}{KCNO} & + H_2O \end{array}$$

Cyanic Acid.

If in carbonic acid, HO . COOH, we conceive the carboxyl group to be replaced by an equivalent cyanogen radical, we obtain the acid cyanic acid $HO.C\vdots N$. This acid, therefore,

bears the same relation to carbonic acid as hydrocyanic acid does to formic acid.

The cyanates contain one oxygen atom more than the cyanides, and may frequently be prepared from the latter by direct oxidation. Thus when potassium cyanide is fused with lead monoxide it reduces the oxide and is itself converted into cyanate—

$$KCN + PbO = Pb + KCNO.$$

The connection between cyanic acid and carbonic acid is practically shown by the behaviour of potassium cyanate, which in solution becomes hydrolysed and converted into a mixture of potassium carbonate and ammonium carbonate—

$$2KCNO + 4H_2O = K_2CO_3 + (NH_4)_2CO_3.$$

Ammonium cyanate, NH_4OCN.—This substance is of great historical interest owing to a peculiar isomeric transformation which it undergoes. It may be prepared as a solid by bringing together ammonia gas and the vapour of cyanic acid at a low temperature. When absolutely dry, it may be kept practically unchanged for a long time at the ordinary temperature. If, however, it is warmed, it passes rapidly into urea, which has the same composition but a different constitution—

$$\underset{\text{Ammonium cyanate}}{NH_4.O.C\vdots N} = \underset{\text{Urea}}{NH_2.CO.NH_2.}$$

The same action takes place readily at the ordinary temperature in aqueous solution. If, therefore, we evaporate a mixed solution containing potassium cyanate and ammonium sulphate we obtain in the residue potassium sulphate and urea. The formation of urea in this way by Wöhler in 1828 was the first example of the artificial preparation of an organic compound produced normally in the living organism.

Carbamide or Urea, $CO(NH_2)_2$.

Nitrogen is excreted from the animal body chiefly in the form of urea, which occurs to the extent of 2 or 3 per cent. in human urine. If urine is evaporated to dryness and the residue extracted with boiling acetone, urea crystallises from the liquid in long needles on cooling. Urea dissolves very

readily in water, and is also easily soluble in alcohol. It may thus, for example, be separated by means of alcohol from the potassium sulphate formed along with it on the evaporation of potassium cyanate and ammonium sulphate, potassium sulphate being insoluble in alcohol. It melts at about 132° and begins to decompose at this temperature, the decomposition taking place rapidly when the temperature is still further raised. The chief products of decomposition are ammonia, carbon dioxide, biuret, and cyanuric acid.

The constitutional formula assigned to urea is as follows:—

$$\underset{\text{Carbonic acid}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{O{-}H}\\ \mathrm{O{-}H}\end{matrix}\right.} \qquad\qquad \underset{\text{Carbamide}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH_2}\end{matrix}\right.}$$

We see that it is derived from carbonic acid by the substitution of two amino groups for the two hydroxyl groups of the latter. It is therefore frequently termed *carbamide*, as it is an amide of carbonic acid. Carbonyl chloride, $COCl_2$, is the acid chloride of carbonic acid. When brought into contact with ammonia gas it produces at once urea according to the following equation:—

$$\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{Cl}\\ \mathrm{Cl}\end{matrix}\right. + \begin{matrix}\mathrm{H.NH_2}\\ \mathrm{H.NH_2}\end{matrix} = \mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH_2}\end{matrix}\right. + \begin{matrix}\mathrm{HCl}\\ \mathrm{HCl}\end{matrix}$$

The relationship of urea to carbonic acid is also proved by boiling the solution with an alkali, a carbonate and ammonia being produced—

$$\underset{\text{Carbamide}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH_2}\end{matrix}\right.} + 2\mathrm{KOH} = \underset{\text{Potassium carbonate}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{OK}\\ \mathrm{OK}\end{matrix}\right.} + 2\mathrm{NH_3}$$

Under the action of certain ferments also, urea is readily converted into ammonium carbonate—

$$\underset{\text{Carbamide}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH_2}\end{matrix}\right.} + 2\mathrm{H_2O} = \underset{\text{Ammonium carbonate}}{\mathrm{O{=}C}\left\langle\begin{matrix}\mathrm{O.NH_4}\\ \mathrm{O.NH_4}\end{matrix}\right.}$$

Urea contains the two residues, NH_2, derived from ammonia. We might, therefore, expect it to display some of the basic

characters of ammonia. In reality it acts as a very feeble monacid base, forming a series of salts such as urea hydrochloride, $CO(NH_2)_2,HCl$; urea nitrate $CO(NH_2)_2,HNO_3$. These salts are soluble in water; the oxalate, $2CO(NH_2)_2,H_2C_2O_4$, however, is sparingly soluble, its formation from urea and oxalic acid solution being sometimes used as a test for urea. It should be noted that although the nitrate is soluble in water, it is very slightly soluble in concentrated nitric acid, so that urea may be separated as nitrate from a moderately concentrated solution by the addition of excess of concentrated nitric acid.

When sodium hypobromite acts upon a solution of ammonia the latter is oxidised with formation of nitrogen and water—

$$3NaBrO + 2NH_3 = N_2 + 3NaBr + 3H_2O.$$

In the same way the amino groups of urea may be oxidised by means of sodium hypobromite to nitrogen and water, the carbonyl group CO being oxidised at the same time to carbon dioxide, which remains dissolved in the excess of caustic soda, always present in an ordinary solution of hypobromite. The reaction may be thus represented by the equation—

$$3NaBrO + \underset{60\text{ g.}}{CO(NH_2)_2} + 2NaOH = \underset{22\cdot4\text{ litres}}{N_2} + 3NaBr + Na_2CO_3 + 3H_2O.$$

This action is of importance as affording a simple and sufficiently accurate method of estimating urea for clinical purposes. The volume of the nitrogen which is given off from a urea solution may be easily measured, and so the concentration of the urea determined from the above equation. Theoretically, 60 grams of urea should yield 22·4 litres of nitrogen at normal temperature and pressure. Owing to secondary reactions a somewhat smaller quantity of nitrogen is obtained. If allowance is made for this loss by the addition of 5 per cent. to the volume of nitrogen actually measured, the results are sufficiently accurate.

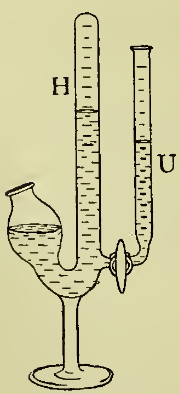


FIG. 21.

A special instrument or ureometer made for the purpose of estimating urea in urine is shown in Fig. 21. A measured volume of urine contained in the limb U is

admitted through the tap into the wider limb H, which is filled with hypobromite solution. The nitrogen collects in H and may be at once measured.

It has already been stated that if urea is heated above its melting-point it decomposes with evolution of ammonia. The substance first produced by this decomposition is known as biuret, and its formation may be expressed by means of the following equation:—

$$NH_2.CO.NH_2 + NH_2.CO.NH_2 = \underset{\text{Biuret}}{NH_2.CO.NH.CO.NH_2} + NH_3.$$

If the heating is continued, a larger proportion of the ammonia is lost, and the resulting substance is cyanuric acid—

$$3NH_2.CO.NH_2 = \underset{\text{Cyanuric acid}}{H_3C_3N_3O_3} + 3NH_3.$$

Biuret, $NH_2.CO.NH.CO.NH_2$.

This substance is chiefly interesting owing to a colour reaction which it gives with copper sulphate and an alkali. If to a solution of biuret a little caustic soda is added and then one or two drops of copper sulphate solution, a bright pink solution is obtained, since biuret, like ammonia, prevents the precipitation of the copper sulphate, the colour of the resulting solution, however, being easily distinguished from the bright blue given by ammonia. This biuret reaction may be used as a test for urea. The dry urea is heated in a test-tube above its melting-point till a certain quantity of ammonia is evolved. After cooling, the residue is dissolved in water and the biuret test applied. The biuret test seems to be given by all substances which contain two $.CO.NH.$ groups, either joined together by their carbon atoms or by an intermediary nitrogen or carbon atom. Many of the polypeptides and proteins consequently give a biuret reaction, which thus forms a valuable test for these important physiological substances.

Cyanuric Acid, $H_3{}^{\cdot}O_3C_3N_3{}'''$.

This solid tribasic acid may be looked upon as a polymer of cyanic acid, $HO.CN$, which is liquid at the ordinary tempera-

ture. When the anhydrous acid is heated it vaporises, not as cyanuric acid, but as cyanic acid—

$$\underset{\text{Cyanuric acid}}{H_3O_3C_3N_3} \rightleftharpoons \underset{\text{Cyanic acid}}{3HOCN.}$$

This is the simplest method for the preparation of the somewhat unstable cyanic acid.

Cyanogen Chloride, CN . Cl.

This substance is the acid chloride of cyanic acid, and may be prepared by the action of chlorine on hydrocyanic acid—

$$Cl_2 + HCN = HCl + CN.Cl.$$

It is a liquid which boils at 15°, the vapour from it being excessively poisonous. With caustic potash it yields potassium cyanate and potassium chloride—

$$CNCl + 2KOH = KCl + KOCN + H_2O.$$

When ammonia acts upon cyanogen chloride the chlorine atom is replaced by the amino group, thus :—

$$CN.Cl + NH_3 = \underset{\text{Cyanamide}}{CN.NH_2} + HCl.$$

Cyanamide, CN . NH$_2$.

Cyanamide is a colourless solid of low melting-point, and both its hydrogen atoms are replaceable by metals. Thus, when brought into contact with a solution of silver nitrate it gives a precipitate of *silver cyanamide*, CN_2Ag_2. The corresponding calcium compound, *calcium cyanamide*, CN . NCa, is prepared on a large scale by heating calcium carbide to bright redness in an atmosphere of nitrogen—

$$CaC_2 + N_2 = \underset{\text{Calcium cyanamide}}{Ca:N.C\vdots N} + C.$$

This substance is of considerable importance as a nitrogenous fertiliser, as it is gradually acted on by water with ultimate production of calcium carbonate and ammonia—

$$CaN.CN + 3H_2O = CaCO_3 + 2NH_3.$$

It is also used as a source of cyanides, for, when heated with

carbon and sodium carbonate, calcium carbonate and sodium cyanide are produced—

$$CaN.CN + C + Na_2CO_3 = 2NaCN + CaCO_3.$$

Alkyl Isocyanates.

The esters of cyanic acid, of the general formula R.OCN, have not as yet been prepared in a state of purity. When a metallic cyanate is made to react with an alkyl iodide, a substance is produced which may be regarded as isomeric with an alkyl cyanate. It is generally termed an **isocyanate**, and by its mode of decomposition it is practically certain that the alkyl group is united, not to oxygen, but to nitrogen. It may be regarded, therefore, as a derivative of isocyanic acid, H.N:C:O.

For example, ethyl iodide reacts with silver cyanate as follows:—

$$C_2H_5I + AgCNO = C_2H_5.N:C:O + AgI.$$

The ethyl isocyanate thus produced is a strongly smelling liquid which boils at 60°. When warmed with caustic soda it decomposes with formation of ethylamine and sodium carbonate—

$$\underset{\text{Ethyl isocyanate}}{C_2H_5.N:C:O} + 2NaOH = \underset{\text{Ethylamine}}{C_2H_5.NH_2} + Na_2CO_3.$$

It unites readily with alcohols to form substituted esters of carbamic acid, which are also known as urethanes (see below)—

$$\underset{\text{Ethyl isocyanate}}{CO:N.C_2H_5} + C_2H_5.OH = \underset{\text{Ethyl urethane}}{NHC_2H_5.CO.OC_2H_5}.$$

Carbamic Acid.

This acid is intermediate between carbonic acid and its diamide. It may therefore be looked upon as the mono-amide of carbonic acid; the relation which it bears to the two substances is clearly seen in the following formula:—

$$\underset{\text{Carbonic acid}}{HO.CO.OH} \qquad \underset{\text{Carbamic acid}}{NH_2.CO.OH} \qquad \underset{\text{Carbamide}}{NH_2.CO.NH_2}.$$

Carbamic acid itself has never been prepared in the free state.

Some of its salts are known, however, and its replaced esters or urethanes are, as stated above, formed by the action of ammonia on alkyl isocyanates.

When carbon dioxide is brought into contact with twice its own volume of ammonia, the gases unite to form *ammonium carbamate*—

$$2NH_3 + CO_2 = NH_2.CO.ONH_4.$$

Ammonium carbamate is a white solid which dissolves in water and is partly converted in solution into ammonium carbonate. It is one of the chief constituents of commercial ammonium carbonate.

Urethanes.—Ethyl carbamate, or **urethane**, $NH_2.CO.OC_2H_5$, is used in medicine as a hypnotic. It is a colourless crystalline substance freely soluble in water, which may be prepared by the action of ammonia on ethyl carbonate—

$$C_2H_5O.CO.OC_2H_5 + NH_3 = NH_2.CO.OC_2H_5 + C_2H_5OH.$$

Secondary amyl carbamate, or **hedonal**,

$$NH_2.CO.OCH(CH_3)(CH_2.CH_2.CH_3),$$

and phenyl-urethane, or **euphorine**, $NHC_6H_5.CO.OC_2H_5$, are similarly employed.

Thiocyanates and Thiourea.

If carbon disulphide is warmed with an alcoholic solution of ammonia, the following reaction takes place :—

$$2NH_3 + CS_2 = \underset{\substack{\text{Ammonium}\\\text{thiocyanate}}}{NH_4.SCN} + H_2S.$$

Ammonium thiocyanate is prepared commercially as a by-product in the manufacture of cyanides by certain processes, and also in gas-works during the purification of coal-gas. The corresponding potassium salt may be made by fusing potassium cyanide with sulphur—

$$KCN + S = KCNS.$$

Thiocyanates are found in traces in the saliva. Solutions of these thiocyanates are used in analysis to test for the presence

of ferric iron, *ferric thiocyanate* forming a deep blood-red solution, the colour of which is not discharged by acids. *Silver thiocyanate*, like silver chloride, is insoluble in water and in acids. *Mercuric thiocyanate*, $Hg(SCN)_2$, which may be prepared by precipitating a solution of mercuric chloride with potassium thiocyanate, is a greyish white amorphous solid, which when dried is combustible, and burns with production of a very voluminous ash, which assumes the form of coiled cylindrical masses known as "Pharaoh's serpents."

When potassium thiocyanate is heated with ethyl iodide, double decomposition takes place with formation of **ethyl thiocyanate**—

$$KSCN + C_2H_5I = C_2H_5SCN + KI.$$

This substance has the constitutional formula $C_2H_5.S.CN$. When heated to a temperature of about 200°, it undergoes an isomeric change into **ethyl isothiocyanate**, which has the constitution $C_2H_5N:C:S$. When the isothiocyanate is heated with dilute acid, it is hydrolysed with production of ethylamine, carbon dioxide, and sulphuretted hydrogen—

$$C_2H_5N:C:S + 2H_2O = C_2H_5.NH_2 + CO_2 + SH_2.$$

This reaction shows that in it the alkyl group is united to nitrogen. **Allyl isothiocyanate**, C_3H_5NCS, occurs in mustard oil, and like the other volatile isothiocyanates has a very strong, penetrating odour.

Thiourea, $CS(NH_2)_2$.—Just as ammonium cyanate passes into the isomeric substance urea, so ammonium thiocyanate passes into the isomeric thiourea, although not so readily—

$$NH_4SCN \rightleftharpoons CS(NH_2)_2.$$

Thiourea is prepared by heating ammonium thiocyanate for some time to a temperature of 170°. It is a crystalline substance with very feeble basic properties.

Guanidine, $NH_2.C(NH).NH_2$.

In this substance all the oxygen radicals of carbonic acid have been replaced by corresponding nitrogen radicals. Guanidine is related to urea by having the imino group $:NH$

instead of the dyad oxygen atom. It may be prepared in the form of its chloride by heating cyanamide with ammonium chloride—

$$\underset{\text{Cyanamide}}{CN.NH_2} + NH_4Cl = \underset{\text{Guanidine chloride}}{NH_2.C(NH).NH_3Cl.}$$

It is generally prepared, however, by heating ammonium thiocyanate for a considerable period at 180°. The thiocyanate is partially converted into thiourea, which loses sulphuretted hydrogen and becomes cyanamide—

$$NH_2.CS.NH_2 = CN.NH_2 + H_2S.$$

The cyanamide formed then reacts with unchanged ammonium thiocyanate to produce guanidine thiocyanate—

$$CN.NH_2 + NH_4SCN = \underset{\text{Guanidine thiocyanate}}{NH_2.C(NH).NH_3SCN.}$$

The base itself, prepared from either of these salts, is a crystalline substance much more strongly basic in character than urea. It acts as a monacid base, and is capable of absorbing carbon dioxide from the air.

Guanidine may be nitrated like an aromatic compound by a mixture of concentrated nitric and sulphuric acids, with formation of a substance called nitroguanidine, which when reduced yields the corresponding aminoguanidine. This on hydrolysis by means of dilute acid breaks up into carbon dioxide and the chlorides of ammonia and of hydrazine. The following equations represent these reactions :—

$$\underset{\text{Guanidine}}{NH_2.C(NH).NH_2} + HO.NO_2 = \underset{\text{Nitroguanidine}}{NH_2.C(NH).NH.NO_2} + H_2O$$

$$\underset{\text{Nitroguanidine}}{NH_2.C(NH).NH.NO_2} + 6(H) = \underset{\text{Aminoguanidine}}{NH_2.C(NH).NH.NH_2} + 2H_2O$$

$$\underset{\text{Aminoguanidine}}{NH_2.C(NH).NH.NH_2} + 2H_2O + 3HCl = \underset{\text{Hydrazine chloride}}{NH_2.NH_3Cl} + 2NH_4Cl + CO_2$$

This method is the most convenient for preparing salts of hydrazine.

PRIMARY AMINES.

Primary amines are substances which may be regarded as being derived from ammonia by the replacement of one of the hydrogen atoms of ammonia by a hydrocarbon radical. Or, looked at from another point of view, they are compounds of a hydrocarbon radical with the amino group NH_2. Thus the compound $CH_3.NH_2$ is an example of such a primary amine, and is known as methylamine. It might appropriately be called methyl ammonia, but for purposes of systematic nomenclature the word ammonia is not used, the term amine being employed in its stead.

The primary amines may be obtained by various methods. For example, they are produced if a nitro- substance is reduced by means of nascent hydrogen (say from zinc or tin and hydrochloric acid). Thus from nitromethane, methylamine may be obtained, and from nitrobenzene the primary amine, phenylamine, or aniline—

$$\underset{\text{Nitromethane}}{CH_3.NO_2} + 6(H) = \underset{\text{Methylamine}}{CH_3.NH_2} + 2H_2O$$

$$\underset{\text{Nitrobenzene}}{C_6H_5.NO_2} + 6(H) = \underset{\text{Aniline}}{C_6H_5.NH_2} + 2H_2O$$

This method of preparation, though of little use for fatty amines, is that chiefly employed for the preparation of aromatic amines.

Again, oximes yield primary amines on reduction with nascent hydrogen, *e.g.*—

$$\underset{\text{Acetoxime}}{CH_3.CH:NOH} + 4(H) = \underset{\text{Ethylamine}}{CH_3.CH_2.NH_2} + H_2O,$$

and it has already been stated that alkyl cyanides may also be reduced to the same class of substances—

$$\underset{\text{Methyl cyanide}}{CH_3.CN} + 4(H) = \underset{\text{Ethylamine}}{CH_3.CH_2.NH_2}.$$

The amines may be derived from ammonia by the action of an alcohol, or more readily of the halogen compound of an alkyl. If the halogen compound of an alkyl is employed, the reaction is one of simple addition—

$$\underset{\text{Ethyl bromide}}{C_2H_5Br} + NH_3 = \underset{\text{Ethyl-ammonium bromide}}{C_2H_5NH_3{}^{\cdot}Br'}.$$

The ammonia here combines directly with the ethyl bromide to form the salt ethyl-ammonium bromine, which, when boiled with a solution of an alkali, decomposes in exactly the same way as ammonium bromide, the place of the ammonia, however, being taken by ethylamine—

$$NH_4Br + NaOH = NaBr + NH_3 + H_2O$$
$$\underset{\text{Ethyl-ammonium bromide}}{NH_3(C_2H_5)Br} + NaOH = NaBr + \underset{\text{Ethylamine}}{NH_2.C_2H_5} + H_2O$$

Primary bases may also be obtained from acid amides by the action of bromine and caustic potash—

$$\underset{\text{Acetamide}}{CH_3.CO.NH_2} + Br_2 + 4KOH = \underset{\text{Methylamine}}{CH_3.NH_2} + 2KBr + K_2CO_3 + 2H_2O.$$

The mechanism of this reaction is somewhat complicated, but it will be seen that it is essentially one of oxidation, the final result being the oxidation and removal of the CO group of the amide as CO_2, which unites with the alkali to form carbonate.

We have already seen that an alkyl isocyanate on treatment with alkali decomposes with formation of potassium carbonate and a primary amine—

$$\underset{\text{Ethyl isocyanate}}{C_2H_5.N:C:O} + 2KOH = \underset{\text{Ethylamine}}{C_2H_5.NH_2} + K_2CO_3.$$

The primary amines resemble ammonia closely in their properties. They possess a smell resembling that of ammonia, although distinguishable from it. Like ammonia, the lower members of the series dissolve readily in water, forming alkaline solutions. They unite readily with acids to form salts resembling the ammonium salts; for example—

$$NH_3 + HCl = NH_4{}^{\cdot}Cl'$$
$$\underset{\text{Ethylamine}}{NH_2(C_2H_5)} + HCl = \underset{\text{Ethyl-ammonium chloride}}{NH_3(C_2H_5){}^{\cdot}Cl'}$$

and from these salts they may be regenerated by boiling the solutions with alkalies.

The following table gives the names, formulæ, and boiling-points of the lower normal members of the fatty series of primary amines:—

		B. Pt.
Methylamine . . .	$CH_3.NH_2$	$-6°$
Ethylamine . . .	$C_2H_5.NH_2$	$+19°$
Propylamine . . .	$C_3H_7.NH_2$	$49°$
Butylamine . . .	$C_4H_9.NH_2$	$76°$

These primary amines are related to the alcohols by the substitution of the amino group, NH_2, for the hydroxyl group, OH, and they may be converted into the corresponding alcohols by the action of nitrous acid. The nature of this action may most readily be made clear by considering the action of nitrous acid on ammonia. When nitrous acid reacts with ammonia the first action, no doubt, is that ammonium nitrite is produced—

$$NH_3 + HNO_2 = NH_4NO_2.$$

Ammonium nitrite, however, is an unstable substance, and readily breaks up into nitrogen and two molecules of water—

$$NH_4NO_2 = N_2 + 2H_2O.$$

Now the action of nitrous acid on a primary amine like ethylamine is similar. It first of all combines with the amine to produce ethyl-ammonium nitrite—

$$NH_2C_2H_5 + HNO_2 = NH_3(C_2H_5)NO_2,$$

which, being unstable like ammonium nitrite, breaks up into nitrogen, ethyl alcohol, and water—

$$NH_3(C_2H_5)NO_2 = N_2 + H_2O + C_2H_5OH.$$

The total result, therefore, is that the amino group is replaced by the hydroxyl group, nitrogen and water being formed at the same time, thus—

$$C_2H_5NH_2 + HNO_2 = C_2H_5OH + N_2 + H_2O.$$

Nitrous acid is itself an unstable substance. It is therefore added to the amine not directly, but by leading nitrogen trioxide

gas into an aqueous solution of the base, or by mixing the aqueous solution with a nitrite, an acid being afterwards added to liberate nitrous acid from the latter—

$$\underset{\text{Ethylamine}}{C_2H_5.NH_2} + KNO_2 + HCl = \underset{\text{Ethyl alcohol}}{C_2H_5OH} + N_2 + H_2O + KCl.$$

In the case of aromatic primary amines, the action of nitrous acid is somewhat different if the solutions are kept cold. Diazo-substances are produced which, however, readily break up on heating with water, yielding nitrogen and hydroxyl derivatives. These diazo- compounds will be considered in a subsequent section.

A characteristic test for primary amines is the production of isonitriles (p. 223) by the joint action of chloroform and alcoholic potash. Thus, if aniline is subjected to the action of these substances phenyl-carbylamine is produced, according to the following equation, and may be at once recognised by its powerful and unpleasant odour—

$$\underset{\text{Phenylamine}}{C_6H_5.NH_2} + CHCl_3 + 3KOH = \underset{\text{Phenyl-carbylamine}}{C_6H_5.NC} + 3KCl + 3H_2O.$$

Care must be taken in performing this test, owing to the poisonous nature of the carbylamines.

Glucosamine has the following constitutional formula:—

$$CH_2OH.\mathbf{C}HOH.\mathbf{C}HOH.\mathbf{C}HOH.\mathbf{C}HNH_2.CHO,$$

and is a primary amine intimately related to glucose, the hydroxyl group of glucose next to the aldehyde group being replaced by NH_2. It is a product of the hydrolysis of certain proteins, and its relationship with glucose is shown by the fact that it yields glucosazone when heated with phenyl-hydrazine.

PRIMARY DIAMINES.

The primary monamines of the fatty series such as methyl-amine, ethylamine, etc., are of little importance from a medical point of view. Some diamines, however, are of considerable importance.

Ethylene-diamine, $NH_2.CH_2.CH_2.NH_2$.—If ammonia in

alcoholic solution is heated with ethylene bromide to 100°, the bromide of ethylene-diamine is produced—

$$2NH_3 + Br.CH_2.CH_2.Br = \underset{\text{Ethylene-diammonium-dibromide}}{NH_3Br.CH_2.CH_2.NH_3Br.}$$

The base ethylene-diamine, derived from this substance by the action of alkali, is a liquid which boils at 116°. When its chloride is heated, ammonia and hydrochloric acid are evolved and a substance named piperazine is produced—

$$2\begin{array}{l}CH_2—NH_2\\ |\\ CH_2—NH_2\end{array} = \underset{\text{Piperazine}}{\begin{array}{lcl}CH_2—NH—CH_2\\ | & & |\\ CH_2—NH—CH_2\end{array}} + 2NH_3$$

Tetramethylene-diamine, $NH_2.(CH_2)_4.NH_2$.—This substance may be prepared by the reduction of ethylene cyanide, formed from ethylene dibromide and potassium cyanide—

$$Br.CH_2.CH_2.Br + 2KCN = \underset{\text{Ethylene-dicyanide}}{NC.CH_2.CH_2.CN} + 2KBr$$

$$NC.CH_2.CH_2.CN + 8(H) = \underset{\text{Tetramethylene-diamine}}{NH_2.CH_2.CH_2.CH_2.CH_2.NH_2}$$

It is also produced during the putrefaction of flesh, and is known as **putrescine.** When heated, it gives off ammonia and is converted into pyrrolidine (p. 275)—

$$\begin{array}{l}CH_2—CH_2—NH_2\\ |\\ CH_2—CH_2—NH_2\end{array} = \underset{\text{Pyrrolidine}}{\begin{array}{l}CH_2—CH_2\\ |\\ CH_2—CH_2\end{array}\!\!>NH} + NH_3$$

Pentamethylene-diamine, $NH_2.(CH_2)_5.NH_2$.—This substance may be prepared by the reduction of trimethylene cyanide, $CN.CH_2.CH_2.CH_2.CN$. Like putrescine, it is formed during the putrefaction of albuminous bodies, and is then known as **cadaverine.** When its hydrochloride is heated, ammonia is given off and piperidine results—

$$CH_2\!<\!\begin{array}{l}CH_2—CH_2—NH_2\\ CH_2—CH_2—NH_2\end{array} = \underset{\text{Piperidine}}{CH_2\!<\!\begin{array}{l}CH_2—CH_2\\ CH_2—CH_2\end{array}\!\!>NH} + NH_3$$

These diamines are diacid bases, uniting with two molecules of a monobasic acid, or one molecule of a dibasic acid, to form normal salts. They are highly poisonous, and are examples of the class of substance known as **ptomaines.**

AROMATIC AMINES.

Many of the aromatic amines are of great importance, not so much on their own account, as being stages in the preparation of substances that are required for the production of drugs, and more particularly of stains and dyes.

Aniline, $C_6H_5NH_2$.—Aniline is prepared commercially by the reduction of nitrobenzene by means of the nascent hydrogen derived from iron and hydrochloric acid. The aniline being a base, unites with some of the hydrochloric acid present. When the reduction is complete, therefore, milk of lime is added to liberate the base, which can then be distilled over by means of steam, with which it is volatile, and afterwards separated and purified by fractional distillation.

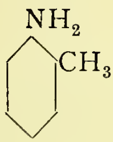
In the pure state aniline is a colourless, strongly refractive liquid which boils at 189°; owing to oxidation, however, it is generally coloured yellow or red. It has a specific gravity slightly greater than that of water, in which it is only slightly soluble. It dissolves readily in aqueous solutions of acids to form salts—

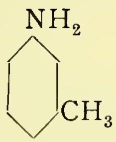
$$C_6H_5.NH_2 + HCl = \underset{\text{Aniline chloride *}}{C_6H_5.NH_3Cl.}$$

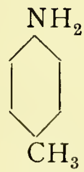
It is a very feeble base, much feebler than ammonia or the fatty primary amines, being comparable amongst bases to phenol amongst acids. Its salts generally crystallise well. It can readily be detected by means of a hypochlorite solution (for example, bleaching powder solution), which yields a deep violet coloration, turning afterwards to a dirty reddish colour.

* This salt is often termed aniline *hydrochloride*, being an addition compound of aniline and hydrochloric acid. Since, however, the corresponding nitrate, $C_6H_5.NH_3NO_3$, and similar salts are termed simply aniline nitrate, sulphate, etc., the name aniline *chloride* may be used with equal propriety.

Toluidines, $CH_3 . C_6H_4 . NH_2$.—There are three toluidines, which are represented by the following formulæ :—


o-Toluidine


m-Toluidine


p-Toluidine

These may be prepared by the reduction of the corresponding nitro- compounds. In their properties they resemble aniline, being feeble bases very sparingly soluble in water. Ortho- and meta-toluidine are liquid; para-toluidine is a solid, melting at 45°.

Phenylene-diamines, $NH_2 . C_6H_4 . NH_2$.—These diamines are produced by the reduction of the corresponding dinitro-compounds. The meta- and para-phenylene-diamines are used in the production of dyes, and the former is specially useful in testing for nitrites, a mere trace of nitrous acid turning its solution a bright yellow colour (p. 321).

SECONDARY AMINES.

If two of the hydrogen atoms of ammonia are replaced by alkyl groups, secondary amines result. Thus, in the secondary amine dimethylamine, $(CH_3)_2NH$, two of the hydrogen atoms of ammonia are replaced by two methyl groups. These substances are sometimes termed imino bases, since they contain the dyad imino group NH.

Secondary amines are formed together with primary amines when an alkyl iodide is made to interact with an alcoholic solution of ammonia. Thus, from ammonia and ethyl bromide we not only obtain ethyl-ammonium bromide, but also diethyl-ammonium bromide, $NH_2(C_2H_5)_2Br$. We may suppose this substance to be formed by the action of ethyl bromide upon ethyl-ammonium bromide—

$$NH_3C_2H_5 . Br + C_2H_5Br = NH_2(C_2H_5)_2Br + HBr.$$

When warmed with a solution of potash, diethyl-ammonium bromide is decomposed with liberation of diethylamine—

$$\underset{\text{Diethyl-ammonium bromide}}{NH_2(C_2H_5)_2Br} + KOH = \underset{\text{Diethylamine}}{NH(C_2H_5)_2} + KBr + H_2O.$$

The secondary amines may be distinguished and separated from the primary amines by the action of nitrous acid. As we have seen, nitrous acid, derived from potassium nitrite and hydrochloric acid, acts upon primary amines with evolution of nitrogen and production of an alcohol. The action of nitrous acid on secondary amines is entirely different. Diethylamine, for example, when treated with nitrous acid reacts according to the following equation:—

$$(C_2H_5)_2NH + HO.NO = \underset{\text{Diethyl-nitrosamine}}{(C_2H_5)_2N.N:O} + H_2O,$$

with formation of an oily substance known as a **nitrosamine.** Since this nitrosamine is insoluble in water it may be readily separated from the soluble ethyl alcohol produced simultaneously from ethylamine. The secondary base may be recovered as chloride from the nitrosamine by heating with concentrated hydrochloric acid—

$$\underset{\text{Diethyl-nitrosamine}}{(C_2H_5)_2N.NO} + HCl = \underset{\text{Diethylamine}}{(C_2H_5)_2NH} + \underset{\text{Nitrosyl chloride}}{NOCl.}$$

The secondary bases may further be distinguished from the primary bases by their not giving the carbylamine test with chloroform and alcoholic potash (p. 238).

The secondary bases unite with one molecule of a monobasic acid to form salts, and indeed in their ordinary properties resemble the primary bases closely. The secondary bases of the fatty series are relatively unimportant, but some secondary bases containing aromatic radicals are of considerable importance.

Methyl-aniline, *methyl-phenylamine,* $(C_6H_5)(CH_3)NH$.—This substance may be prepared together with dimethyl-aniline, by heating aniline chloride with methyl alcohol under pressure—

$$C_6H_5.NH_2 + CH_3OH = \underset{\text{Methyl-aniline}}{(C_6H_5)(CH_3)NH} + H_2O.$$

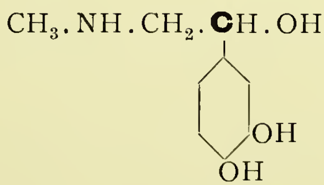
On addition of alkali to the solution of the chloride, the base is precipitated as an insoluble oil. It resembles aniline in its properties, and is used in the manufacture of dyes. Solutions of its salts readily yield a yellow oily nitrosamine on addition of potassium nitrite.

Diphenylamine, $(C_6H_5)_2NH$.—This substance is formed by heating aniline chloride with aniline at about 250°, when the following reaction takes place :—

$$C_6H_5.NH_3Cl + C_6H_5.NH_2 = \underset{\text{Diphenylamine}}{(C_6H_5)_2NH} + NH_4Cl.$$

Diphenylamine is a solid crystalline substance which melts at 54° and is practically insoluble in water. It is a much weaker base than aniline, and its salts are so readily hydrolysed by water that the base itself, unlike aniline or methyl-aniline, is insoluble in dilute acids. Concentrated solutions of acids, however, dissolve it. Like methyl-aniline, it is extensively used in the preparation of dyes.

Adrenaline, $C_9H_{13}O_3N$, is a secondary amine of great physiological importance. It is secreted by the suprarenal capsules, from which it may be extracted, and has also been prepared synthetically. Its constitutional formula is as follows :—



Adrenaline

From this it may be seen that adrenaline is at once a secondary alcohol, a dihydric phenol, and a secondary base. Being amphoteric, it dissolves in both acids and alkalies. The carbon atom of the secondary alcohol group is asymmetric, so that the substance is capable of existing in dextro- and lævo- modifications. The lævo-rotatory substance alone is found in the suprarenal bodies, and it possesses the physiological property of constricting the blood-vessels in a much greater degree than the dextro- modification. The solution of the chloride $C_9H_{13}O_3N,HCl$ is chiefly employed in medicine.

TERTIARY AMINES.

When ethyl bromide acts upon ammonia, the final product contains not only the bromides of ethylamine and diethylamine, but also of the tertiary base triethylamine, $N(C_2H_5)_3$. As before, this base may be liberated by the action of caustic alkali—

$$N(C_2H_5)_3HBr + KOH = N(C_2H_5)_3 + KBr + H_2O.$$

The tertiary bases of this type resemble closely in their physical properties the primary and secondary bases with an equal number of atoms. They combine readily with one molecule of a monobasic acid to form salts. It should be noted that there is not much difference in basic strength between ammonia on the one hand, and the primary, secondary, or tertiary bases on the other, in which one or more hydrogens of the ammonia are replaced by an equivalent number of alkyl radicals such as ethyl or methyl.

The tertiary bases may be distinguished from the primary and secondary bases by means of nitrous acid, which in the main leaves them unattacked, although they may be in part broken up with formation of a secondary base.

Trimethylamine, $(CH_3)_3N$, occurs in small quantity in many plants, and also in herring-brine, the characteristic odour of which is principally due to trimethylamine. It is prepared commercially together with some dimethylamine by the distillation of the residues from which beet-sugar has been crystallised. It is a gas at the ordinary temperature, but can be reduced to the state of liquid by cooling with ice. It is very soluble in water, and its chloride is used in the industrial preparation of methyl chloride—

$$\underset{\substack{\text{Trimethylamine chloride}\\\text{(Trimethyl-ammonium chloride)}}}{3N(CH_3)_3HCl} = 2CH_3Cl + 2N(CH_3)_3 + \underset{\substack{\text{Methylamine chloride}\\\text{(Methyl-ammonium chloride)}}}{N(CH_3)H_3Cl}.$$

This action is carried out at a temperature of about 300°. The methyl chloride and trimethylamine distil over, whilst methylamine chloride remains as a residue.

Dimethyl-aniline, $C_6H_5.N(CH_3)_2$.—This substance, like

methyl-aniline, is prepared in the form of its chloride by heating aniline chloride with methyl alcohol under pressure—

$$C_6H_5.NH_3Cl + 2CH_3.OH = C_6H_5.N(CH_3)_2HCl + 2H_2O.$$

The chloride is decomposed by milk of lime, and the base is purified by distillation with steam. It is an oil which is practically insoluble in water, and is largely used in the preparation of dyes. It is a feeble base of about the same strength as aniline.

QUATERNARY AMMONIUM HYDROXIDES.

The primary, secondary, and tertiary bases are all of the type of ammonia; that is, they are not bases proper, but their solutions in water, like that of ammonia, have an alkaline reaction due to the formation of an unstable ammonium hydroxide—

$$\begin{array}{lcl} NH_3 + H_2O & \rightleftharpoons & NH_4^{\cdot}OH' \\ NH_2(CH_3) + H_2O & \rightleftharpoons & NH_3(CH_3)^{\cdot}OH' \\ NH(CH_3)_2 + H_2O & \rightleftharpoons & NH_2(CH_3)_2^{\cdot}OH' \\ N(CH_3)_3 + H_2O & \rightleftharpoons & NH(CH_3)_3^{\cdot}OH' \end{array}$$

These ammonium hydroxides decompose on evaporation of the solution into the volatile anhydrous bases and water. The possibility of such a decomposition is absent when all four hydrogens of the ammonium radical are replaced by alkyl groups, so that the quaternary ammonium hydroxides are much more stable non-volatile substances which resemble in their properties the caustic alkalies, sodium hydroxide or potassium hydroxide. They may be prepared as follows:— Tertiary bases combine readily with halogen compounds of the alkyls to form salts. Thus, if triethylamine and ethyl chloride are heated together in a sealed tube, they combine with formation of tetraethyl-ammonium chloride—

$$N(C_2H_5)_3 + C_2H_5Cl = \underset{\text{Tetraethyl-ammonium chloride}}{N(C_2H_5)_4Cl.}$$

This chloride is not decomposed by boiling its aqueous solution with caustic alkali, and so can be readily distinguished

from the chloride of a primary, secondary, or tertiary base. If, however, a solution of the base in absolute ethyl alcohol is prepared and mixed with an alcoholic solution of potassium hydroxide in the same solvent, double decomposition occurs, according to the following equation:—

$$N(C_2H_5)_4Cl + KOH = KCl + N(C_2H_5)_4OH.$$

Potassium chloride being practically insoluble in absolute alcohol, separates as a precipitate, and the remaining solution contains tetraethyl-ammonium hydroxide. If the bulk of the alcohol is now distilled off and water is added, the base crystallises out in the form of a hydrate on concentration of the solution. The same base may be obtained by shaking up an aqueous solution of tetraethyl-ammonium chloride with silver hydroxide—

$$N(C_2H_5)_4Cl + AgOH = AgCl + N(C_2H_5)_4OH.$$

The insoluble silver hydroxide is filtered off and the solution concentrated to the crystallising point. Tetraethyl-ammonium hydroxide is a powerful base like caustic soda or caustic potash. It is extremely soluble in water, and when perfectly pure has no odour, differing in this respect from the primary, secondary, and tertiary bases, which have all an ammoniacal smell. When heated it breaks up into triethylamine and ethyl alcohol—

$$N(C_2H_5)_4OH = N(C_2H_5)_3 + C_2H_5OH.$$

The other quaternary bases resemble tetraethyl-ammonium hydroxide closely in their properties, and need not here be described.

ACID AMIDES AND IMIDES.

When one hydrogen atom of ammonia is replaced by an alkyl group we obtain an amine which, in its general properties, closely resembles ammonia. If instead of replacing a hydrogen atom of ammonia by an alkyl group, we replace it by an acyl group, the substance obtained is much less basic in character than ammonia, and indeed in some cases scarcely possesses basic properties at all, although it still contains the amino group NH_2. The derivatives of ammonia formed in this way by the substitution of acyl groups for the hydrogen of ammonia are called acid amides, or simply **amides**. They may be prepared by a method analogous to the preparation of a primary amine from an alkyl chloride and ammonia. Thus, if acetyl chloride is treated with ammonia, acetyl ammonia or acetamide is produced—

$$CH_3.CO.Cl + NH_3 = \underset{\text{Acetamide}}{CH_3.CO.NH_2} + HCl.$$

This method is a general one for the production of the amides of acids, and we may write the general equation for it as follows:—

$$\underset{\text{Acyl chloride}}{R.CO.Cl} + NH_3 = \underset{\text{Amide}}{R.CO.NH_2} + HCl.$$

Amides may also be prepared by the action of ammonia on esters—

$$\underset{\text{Ethyl ester}}{R.COOC_2H_5} + NH_3 = \underset{\text{Amide}}{R.CO.NH_2} + C_2H_5OH.$$

The amides of acids are produced when the ammonium salts of the acids are heated. Thus, when ammonium acetate is

distilled in a current of ammonia, a large proportion of it is converted into acetamide by loss of water—

$$\underset{\text{Ammonium acetate}}{CH_3.COONH_4} = \underset{\text{Acetamide}}{CH_3.CO.NH_2} + H_2O.$$

The reverse action, namely, the hydrolysis of the amides with production of the acid and ammonia, may be carried out by heating the amide with dilute mineral acid or with alkali—

$$CH_3.CO.NH_2 + H_2O + HCl = CH_3.CO.OH + NH_4Cl.$$

It has already been stated that when the amides are heated with phosphorus pentoxide they lose water and are converted into nitriles—

$$\underset{\text{Acetamide}}{CH_3.CO.NH_2} + P_2O_5 = \underset{\text{Acetonitrile}}{CH_3.CN} + 2HPO_3.$$

Conversely, when a nitrile is hydrolysed by means of acid it is often possible to separate the corresponding amide before complete hydrolysis into the acid and ammonia has taken place—

$$\underset{\text{Acetonitrile}}{CH_3.CN} + H_2O = \underset{\text{Acetamide}}{CH_3.CO.NH_2}.$$

The conversion of the amides into primary amines by means of bromine and caustic potash has already been noted (p. 236).

Formamide, $H.CO.NH_2$, may be prepared by heating ammonium formate—

$$H.COONH_4 = H.CO.NH_2 + H_2O.$$

It is a liquid which freezes at 3° and boils at about 200°. It mixes with water in all proportions, and is sometimes used to dissolve substances which are not readily soluble in other solvents, *e.g.* starch.

Acetamide, $CH_3.CO.NH_2$, is a solid which melts at 82° and boils at 223°. As usually prepared by any of the above methods it has a characteristic smell resembling that of mice, but this odour disappears when the substance is carefully purified. It forms salts with strong mineral acids; for example, hydrochloric acid or nitric acid. These salts, however, are

somewhat unstable, and are almost completely hydrolysed when dissolved in water—

$$\underset{\substack{\text{Acetamide nitrate}\\\text{(Acetyl-ammonium nitrate)}}}{CH_3.CO.NH_3.NO_3} \rightleftharpoons CH_3.CO.NH_2 + HNO_3.$$

Benzamide, $C_6H_5.CO.NH_2$, is a typical aromatic amide, and is usually prepared from benzoyl chloride and ammonium carbonate—

$$C_6H_5.CO.Cl + NH_4HCO_3 = C_6H_5.CO.NH_2 + HCl + CO_2 + H_2O.$$

It is a crystalline solid which melts at 130°, the crystals being freely soluble in hot water, but sparingly soluble in cold water.

Acetanilide, $CH_3.CO.NH.C_6H_5$.—When aniline is substituted for ammonia in the preparation of acetamide, the resulting product is acetanilide, which may be regarded as the phenyl derivative of acetamide, just an aniline is the phenyl derivative of ammonia. It is prepared by boiling together a mixture of aniline and glacial acetic acid in a flask provided with a reflux condenser. Aniline acetate is first formed by the union of aniline and acetic acid, and then gradually loses water with production of acetanilide—

$$\underset{\text{Acetic acid}}{CH_3.COOH} + \underset{\text{Aniline}}{NH_2.C_6H_5} = \underset{\text{Aniline acetate}}{CH_3.COONH_3C_6H_5}.$$

$$\underset{\text{Aniline acetate}}{CH_3.COONH_3C_6H_5} = \underset{\text{Acetanilide}}{CH_3.CO.NHC_6H_5} + H_2O.$$

Acetanilide is sparingly soluble in cold water, but dissolves in boiling water, from which it may be crystallised in the form of shining scales which melt at 112°. It is used as a febrifuge in medicine under the name of **antifebrine**.

Phenacetin, $CH_3.CO.NH.C_6H_4.OC_2H_5$.—This substance is prepared by the prolonged heating of glacial acetic acid and para-ethoxyaniline, or para-phenetidine—

$$\underset{\text{Acetic acid}}{CH_3.COOH} + \underset{p\text{-Phenetidine}}{NH_2.C_6H_4.OC_2H_5} = \underset{\text{Phenacetin}}{CH_3.CO.NH.C_6H_4.OC_2H_5} + H_2O.$$

It is the para-ethoxy derivative of acetanilide, and is much used in medicine to reduce temperature and soothe pain. It forms white, shining crystals which melt at 135°, and are sparingly soluble in water.

AMIDES OF DIBASIC ACIDS.

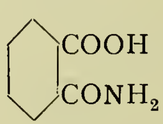
From what has been stated above it may be seen that an amide is related to the corresponding acid by having the amino group NH_2 instead of the hydroxyl OH, which forms part of the carboxyl group. Dibasic acids have two hydroxyl groups, and it is therefore possible to replace them successively by two amino groups. We have already seen an instance of this successive replacement in the case of carbonic acid—

HO.CO.OH	$HO.CO.NH_2$	$NH_2.CO.NH_2$
Carbonic acid	Carbamic acid	Carbamide

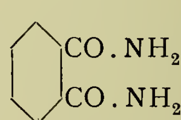
When one of the hydroxyl groups is replaced by the amino group, we obtain a substance intermediate between the dibasic acid and its diamide. Such substances retain the character both of acid and of amide, and are generally called **amic acids.** Thus, from carbonic acid we obtain carbamic acid, the diamide of carbonic acid being carbamide or urea. Similarly, from succinic acid and from phthalic acid we obtain amic acids and diamides, according to the following scheme:—

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.CONH_2 \end{array} \qquad\qquad \begin{array}{l} CH_2.CO.NH_2 \\ | \\ CH_2.CO.NH_2 \end{array}$$

Succinamic acid Succinamide



Phthalamic acid



Phthalamide

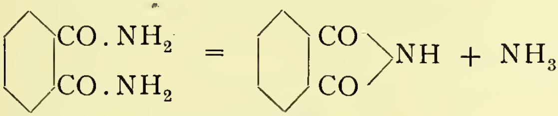
The general properties of the diamides closely resemble those of the amides of monobasic acids.

IMIDES OF DIBASIC ACIDS.

If we heat the diamides of dibasic acids, which, like succinic and phthalic acids, have the two carboxyl groups on neighbouring carbon atoms, they readily lose ammonia and are converted into imides—

$$\begin{array}{l} CH_2.CO.NH_2 \\ | \\ CH_2.CO.NH_2 \end{array} = \begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!\Big\rangle NH + NH_3$$

Succinamide Succinimide

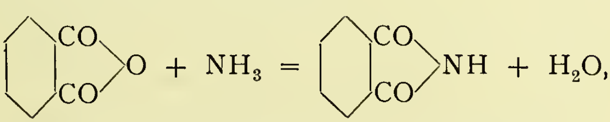


Phthalamide Phthalimide

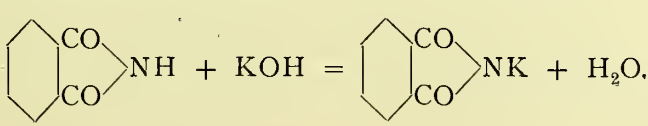
These imides correspond to the secondary amines, or imines, since they contain the dyad imino group :NH. They are practically without basic properties, and indeed may rather be regarded as very feeble acids, the hydrogen of the imino group being replaceable by metals. Thus, if succinimide is evaporated to dryness with an equivalent quantity of potassium hydroxide dissolved in absolute alcohol, a solid residue of potassium succinimide is obtained which contains potassium instead of the hydrogen of the imino group—

$$\begin{array}{l} CH_2—CO \\ | \\ CH_2—CO \end{array}\!\!\Big\rangle NH + KOH = \begin{array}{l} CH_2—CO \\ | \\ CH_2—CO \end{array}\!\!\Big\rangle NK + H_2O.$$

Phthalimide, which is usually prepared by the action of ammonia on phthalic anhydride—



yields potassium phthalimide on similar treatment—

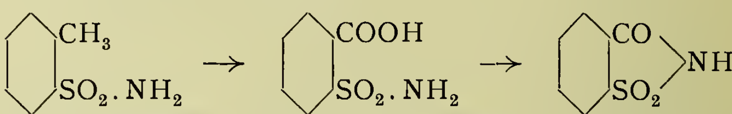


These potassium salts of imides are largely hydrolysed by water, the equations for the reaction being the reverse of those just given.

Saccharin, $C_7H_5O_3NS$.—Sulphonic acids form amides in the same manner as carboxylic acids. For example, benzene-sulphonic acid may be converted by phosphorus pentachloride into benzene-sulphonyl chloride, and this by ammonia into benzene-sulphonamide—

$$\underset{\text{Benzene-sulphonic acid}}{C_6H_5.SO_2.OH} \rightarrow \underset{\text{Benzene-sulphonyl chloride}}{C_6H_5.SO_2Cl} \rightarrow \underset{\text{Benzene-sulphonamide}}{C_6H_5.SO_2.NH_2}.$$

Saccharin is prepared from *o*-toluene-sulphonamide by oxidation with potassium permanganate—



o-Toluene-sulphonamide   *o*-Benzoic acid sulphonamide   Saccharin

The sulphonamide of benzoic acid first produced loses water and forms saccharin, the imide of a mixed carboxylic and sulphonic acid.

Saccharin is sparingly soluble in water, but readily dissolves in alkalies. Both it and its sodium salt $C_6H_4(CO)(SO_2):NNa$ are used as sugar substitutes in cases of diabetes. Pure saccharin has, weight for weight, about five hundred times the sweetening power of cane-sugar.

AMINO ACIDS.

The amino acids must be carefully distinguished from the acid amides. The relationship between these classes of substances is of the same nature as that between chloro acids on the one hand, and acyl chlorides on the other. When acetyl chloride is treated with ammonia an acid amide results; when chloracetic acid is treated with ammonia, the product is an amino acid—

$$\underset{\text{Acetyl chloride}}{CH_3.CO.Cl} + NH_3 = \underset{\text{Acetamide}}{CH_3.CO.NH_2} + HCl$$

$$\underset{\text{Chloracetic acid}}{Cl.CH_2.COOH} + NH_3 = \underset{\text{Amino-acetic acid}}{NH_2.CH_2.COOH} + HCl$$

This method of formation of amino acids from halogen derivatives of the fatty acids is general. The above equation, however, does not truly represent the action of ammonia on chloracetic acid, because the amino acid primarily produced has still acid properties and combines with more ammonia to form an ammonium salt. The complete action may then be represented as follows:—

$$\underset{\text{Ammonium chloracetate}}{Cl.CH_2.COONH_4} + 2NH_3 = \underset{\text{Ammonium amino-acetate}}{NH_2.CH_2.COONH_4} + NH_4Cl.$$

Amino-acetic acid yields a solution which is practically neutral to indicators. It will be observed that, owing to the presence of the carboxyl group in the molecule, it possesses acid properties, whilst the presence of the amino group NH_2 in the molecule confers basic properties upon it. We might expect, therefore, that this and other amino acids would be amphoteric in character; that is, that they might react as acids towards bases and also as bases towards acids. We find, indeed, that the amino acids are capable of reacting with both acids and bases, the types of reaction being exemplified by the following equations:—

$$\underset{\text{Amino-acetic acid}}{NH_2.CH_2.COOH} + NaOH = \underset{\text{Sodium amino-acetate}}{NH_2.CH_2.COONa} + H_2O$$

$$\underset{\text{Amino-acetic acid}}{NH_2.CH_2.COOH} + HCl = \underset{\text{Chloride of amino-acetic acid}}{NH_3Cl.CH_2.COOH}$$

When we consider a molecule which, like that of amino-acetic acid, is acidic in one part and basic in another, we might anticipate that in a solution of the free acid the basic part would act upon the acidic part, and a sort of internal salt result. We have reason to believe that this is so, and that a portion at least of amino-acetic acid in solution exists as a substance having the formula—

$$\overline{NH_3.CH_2.COO},$$

the basic neutralising the acidic part and forming a cyclic compound. From this point of view amino-acetic acid is an internal salt, and being derived from a weak acid and a weak base, such a salt would have a practically neutral reaction, as is actually the case.

Many amino acids, in particular α-amino acids, are of great physiological importance, as they form a large proportion of the hydrolysis products of the proteins found in the animal body. These substances will be dealt with later under the heading of the proteins.

Glycine, *amino-acetic acid*, $NH_2.CH_2.COOH$.—The ammonium salt of this acid may be prepared from chloracetic acid and ammonia, as indicated above. The acid may be conveniently obtained in the form of its chloride by the hydrolysis of hippuric acid (see below) by means of hydrochloric acid. It may also be produced by boiling gelatine with dilute acid. The acid itself is freely soluble in water, from which it separates in crystals melting at 235°. Its solutions are sweet to the taste, as the name indicates.

If glycine is treated with nitrous acid, the amino group NH_2 is exchanged for the hydroxyl group OH, just as in the case of primary amines. We therefore obtain from it hydroxyacetic acid, or glycollic acid, according to the following equation:—

$$\underset{\text{Glycine}}{NH_2.CH_2.COOH} + HNO_2 = \underset{\text{Glycollic acid}}{HO.CH_2.COOH} + N_2 + H_2O.$$

This property it shares with the acid amides, from which, however, it may be distinguished by boiling with caustic alkali. The amides are hydrolysed with evolution of ammonia; glycine is undecomposed by alkali, and no ammonia is produced. Glycine and other amino acids give deep blue solutions with soluble salts of copper. These copper compounds crystallise well, and may be prepared most conveniently by boiling a solution of the amino acid with excess of copper carbonate, filtering and crystallising.

Glycine is not only capable of forming metallic salts, it is also capable of forming esters. If glycine is boiled with ethyl alcohol and a current of hydrogen chloride passed through the boiling solution, it is gradually converted into the chloride of the ethyl ester—

$$NH_2.CH_2.COOH + C_2H_5OH + HCl = NH_3Cl.CH_2.COOC_2H_5 + H_2O.$$

From this hydrochloride the ester can be separated as an oil

by addition of the requisite quantity of alkali to neutralise the acid. The ester can then be purified by distillation under diminished pressure. In it the acid character of the hydroxyl group has been destroyed by its conversion into the ester group, so that the ester possesses only a basic and no acidic character. The esters of the amino acids are of some importance in the process of separating the mixture of amino acids formed by hydrolysis of the proteins.

Hippuric acid, *benzoyl-glycine*, $C_6H_5.CO.NH.CH_2.COOH$.—This substance, as its name indicates, occurs in the urine of horses and of other herbivorous animals. It is a solid crystalline substance which melts at 187°, and is freely soluble in hot water, but very sparingly soluble in cold water. Some of its salts are employed in medicine.

If we consider the formula of hippuric acid—

$$\underset{\text{Benzamide}}{C_6H_5.CO.NH_2} \quad \underset{\text{Hippuric acid}}{C_6H_5.CO.NH.CH_2.COOH} \quad \underset{\text{Glycine}}{NH_2.CH_2.COOH},$$

we see that it may be regarded either as a derivative of benzamide on the one hand, or of glycine on the other. It is therefore related both to an acid amide and to an amino acid. Two methods which may be used for its synthesis show these relationships clearly. First, it may be synthetised by the action of chloracetic acid on benzamide—

$$\underset{\text{Benzamide}}{C_6H_5.CO.NH_2} + \underset{\text{Chloracetic acid}}{Cl.CH_2.COOH} =$$
$$C_6H_5.CO.NH.CH_2.COOH + HCl.$$

Again, it may be produced by the action of benzoyl chloride on glycine—

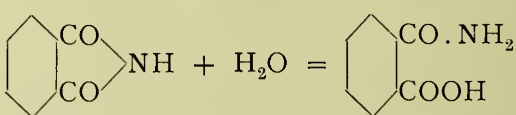
$$\underset{\text{Benzoyl chloride}}{C_6H_5.CO.Cl} + \underset{\text{Glycine}}{NH_2.CH_2.COOH} =$$
$$C_6H_5.CO.NH.CH_2.COOH + HCl.$$

It is generally regarded from the second point of view, since on hydrolysis it decomposes into benzoic acid and glycine—

$$C_6H_5.CO.NH.CH_2.COOH + H_2O =$$
$$C_6H_5.COOH + NH_2.CH_2.COOH.$$

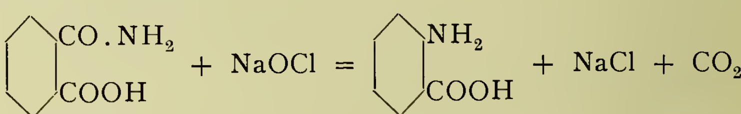
The hydrolysis is conducted by boiling hippuric acid with dilute hydrochloric acid, the glycine being obtained in the form of chloride.

Anthranilic acid, *ortho-amino-benzoic acid*, $NH_2.C_6H_4.COOH$. —This substance may be taken as a typical representative of the aromatic amino acids. It is prepared industrially on a large scale in the synthesis of artificial indigo. When phthalimide is treated with a solution of sodium hypochlorite, it decomposes in a manner analogous to the decomposition of an acid amide, with loss of the group CO and production of a primary amine. We may suppose that the phthalimide is first of all hydrolysed with production of phthalamic acid—



Phthalimide Phthalamic acid

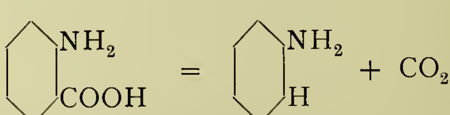
The hypochlorite acting on this substance, like the hypobromite on a simple amide, removes the group CO, according to the following equation:—



Phthalamic acid Anthranilic acid

The amide group $CONH_2$ is thus converted into the primary amino group NH_2.

Anthranilic acid, which was first obtained by the oxidation of indigo, melts at 145°. It is easily soluble in water and in alcohol, has a sweet taste, and decomposes on heating into aniline and carbon dioxide—



Anthranilic acid Aniline

Sarcosine, $NH(CH_3).CH_2.COOH$, is *methyl-glycine*, in which the methyl group replaces a hydrogen atom of the

amino group in the parent substance. It may be prepared by the action of methylamine on chloracetic acid—

$$\underset{\text{Methylamine}}{NH_2CH_3} + \underset{\text{Chloracetic acid}}{Cl.CH_2.COOH} = \underset{\text{Sarcosine}}{NH(CH_3).CH_2.COOH} + HCl.$$

It resembles glycine closely in its properties.

Creatine, $(NH_2)(NH)C.N(CH_3).CH_2.COOH$, is related to sarcosine, from which it may be obtained by the action of cyanamide—

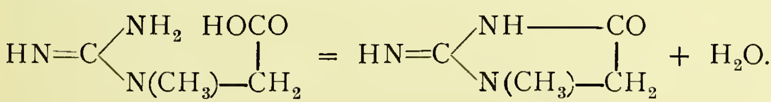
$$\underset{\text{Cyanamide}}{NH_2.CN} + \underset{\text{Sarcosine}}{NH(CH_3).CH_2.COOH}$$
$$= \underset{\text{Creatine}}{(NH_2)(NH)C.N(CH_3).CH_2.COOH.}$$

It is a constituent of muscle, and may conveniently be prepared from meat broth. It crystallises from water in colourless prisms. When boiled with baryta water it is hydrolysed with formation of sarcosine and urea—

$$(NH_2)(NH)C.N(CH_3).CH_2.COOH + H_2O$$
$$= NH_2.CO.NH_2 + NH(CH_3).CH_2.COOH.$$

It may be looked on as a derivative of guanidine, $NH_2.C(NH).NH_2$, in which the two hydrogens of one amino group are replaced by the radicals, CH_3 and $CH_2.COOH$, respectively.

Creatinine is formed from creatine by loss of water—



Creatine Creatinine

The action may be brought about by boiling with acids; and reversal takes place on treatment with alkalies. Creatinine is a normal constituent of urine, and may also be obtained from meat extract. It is much more soluble than creatine, is a well-marked base, and yields crystalline salts with acids. On oxidation with potassium permanganate it yields amongst other products methyl-guanidine, $NH_2.C(NH).NHCH_3$.

Betaine, $\overline{N(CH_3)_3 . CH_2 . COO}$.—Betaine is formed by the action of trimethylamine on chloracetic acid—

$$N(CH_3)_3 + Cl . CH_2 . COOH = \overline{N(CH_3)_3 . CH_2 . COO} + HCl.$$

It may be regarded as trimethyl-glycine, being derived from the closed chain formula of glycine, $\overline{NH_3 . CH_2 . COO}$ by introduction of three methyl groups (*cf.* p. 253). It is contained in many plants, and occurs in considerable quantity in beetroot juice, so that it is found concentrated in the molasses from which beet-sugar has separated. It is very soluble in water, from which it crystallises with one molecule of water of crystallisation, the hydrate probably possessing the formula, $HO . N(CH_3)_3 . CH_2 . COOH$. It is amphoteric, but the salts with acids are the more stable. Thus the chloride $Cl . N(CH_3)_3 . CH_2 . COOH$ crystallises readily from aqueous solution in the anhydrous state.

When heated, betaine decomposes with evolution of trimethylamine, $N(CH_3)_3$, which is commercially prepared by distilling beetroot molasses containing betaine (p. 244).

Choline, $HO . N(CH_3)_3 . CH_2 . CH_2OH$, is the primary alcohol corresponding to the hydrated form of betaine. It occurs widely distributed in the vegetable kingdom in the form of salts, *e.g.*, in hops, cotton-seeds, areca nuts, and certain fungi. In animals it occurs as a constituent of lecithin, and is thus found in brain, egg-yolk, etc. It is a very deliquescent, crystalline mass, the aqueous solution having a strong alkaline reaction in accordance with its constitution as a quaternary base. When oxidised, it yields betaine.

Neurine, $HO . N(CH_3)_3 . CH : CH_2$, is related to choline as ethylene is related to ethyl alcohol. It is formed in the putrefactive decomposition of flesh, and is probably derived from the lecithin contained in the animal tissues. It may be formed by heating choline with baryta water—

$$\underset{\text{Choline}}{HO . N(CH_3)_3 . CH_2 . CH_2OH} = \underset{\text{Neurine}}{HO . N(CH_3)_3 . CH : CH_2} + H_2O.$$

Neurine is a strong poison (ptomaine) in contrast with choline,

which has only slight physiological activity. It is strongly basic, and very soluble in water.

AMINO-DERIVATIVES OF DIBASIC ACIDS.

Aspartic acid, *amino-succinic acid,*

$$COOH.CH_2.\mathbf{C}H(NH_2).COOH,$$

occurs in many plants, and may be obtained as a hydrolysis product of many animal and vegetable proteins. It exists in three modifications, one of which is dextro-rotatory, one lævo-rotatory, and the third the optically inactive mixture of these two acids. On treatment with nitrous acid the varieties of aspartic acid are converted into corresponding malic acids:—

$$\underset{\text{Aspartic acid}}{\begin{array}{l} NH_2.CH.COOH \\ \quad\;\; | \\ \quad\;\; CH_2.COOH \end{array}} + HNO_2 = \underset{\text{Malic acid}}{\begin{array}{l} HO.CH.COOH \\ \quad\;\; | \\ \quad\;\; CH_2.COOH \end{array}} + H_2O + N_2$$

The most important variety of aspartic acid is lævo-rotatory, and is converted into the ordinary lævo-rotatory malic acid. Aspartic acid differs from the amino-derivatives of monobasic acids in being a comparatively strong acid with well-defined metallic salts. The amino group which it contains is only capable of neutralising one of the carboxyl groups of the dibasic acid, the other retaining its acid properties unaltered.

Asparagine, $COOH.\mathbf{C}H(NH_2).CH_2.CONH_2$.—This substance is the monamide of aspartic acid, and occurs in three corresponding modifications. Both the lævo-rotatory and the dextro-rotatory modification occur in plants, but the former is more frequently found. It is generally prepared from asparagus. When hydrolysed by boiling with dilute acids or alkalies, the $CONH_2$ group is converted into the carboxyl group, and aspartic acid results—

$$\underset{\text{Asparagine}}{\begin{array}{l} NH_2.CH.COOH \\ \quad\;\; | \\ \quad\;\; CH_2.CONH_2 \end{array}} + H_2O = \underset{\text{Aspartic acid}}{\begin{array}{l} NH_2.CH.COOH \\ \quad\;\; | \\ \quad\;\; CH_2.COOH \end{array}} + NH_3$$

The NH_2 group, which is attached to the unoxidised carbon atom, is unaffected by the above treatment.

Glutaminic acid, $COOH.CH_2.CH_2.\mathbf{C}H(NH_2).COOH$.— This acid is α-amino-glutaric acid, and resembles aspartic acid closely in its properties. It is a frequent product of the hydrolysis of proteins. Its monamide, **glutamine,** occurs along with asparagine in beetroot and other plants, generally as the inactive modification.

DIAZO COMPOUNDS, HYDRAZINES, AND AZO COMPOUNDS.

Diazo Compounds.

It has already been mentioned that the primary aromatic amines behave, in regard to their action on nitrous acid, differently from the corresponding fatty compounds. If to a solution of aniline chloride we add one equivalent of potassium nitrite and one equivalent of free hydrochloric acid to liberate nitrous acid from its salt, then the following action occurs:—

$$C_6H_5.NH_3.Cl + HNO_2 = C_6H_5.NN.Cl + 2H_2O.$$

The new substance produced is what we call a diazo compound, since it contains two nitrogen atoms directly united together. Two methods of formulating this compound have been proposed, namely:—

$C_6H_5.N:N.Cl$	$C_6H_5.\underset{\vdots}{N}.Cl$ $\quad\quad\;\; N$
Diazobenzene chloride	Phenyl-diazonium chloride

In the first of these formulæ both nitrogen atoms are represented as triad; in the second formula one atom is represented as triad, and the other as pentad. It is possible that two substances possessing these formulæ may exist. To the former we give the name diazobenzene chloride, to the latter the name phenyl-diazonium chloride. The termination of the name diazonium indicates the relationship to ammonium, in the salts of which the nitrogen united to the acid radical is pentad, as it is in the phenyl-diazonium chloride. It is now generally accepted that the substance actually produced from the above reagents has the diazonium constitution.

The diazonium salts are seldom prepared in the pure state,

as they are somewhat unstable compounds, many of them when dry decomposing with explosive violence on heating, or on percussion. They are, as a rule, freely soluble in water, less soluble in alcohol and ether. Their solutions gradually decompose with elimination of nitrogen.

When phenyl-diazonium chloride in aqueous solution is treated with silver hydroxide, it reacts with production of insoluble silver chloride and phenyl-diazonium hydroxide—

$$C_6H_5.N_2.Cl + AgOH = C_6H_5.N_2.OH + AgCl.$$

The solution of the diazonium hydroxide when freed from silver chloride by filtration acts like the solution of a quaternary base. It cannot, however, be separated from solution in the solid state, owing to the ease with which it decomposes.

The diazonium compounds react very readily with other substances, frequently with elimination of nitrogen. Thus, when phenyl-diazonium chloride is heated with water, or more slowly at the ordinary temperature, it reacts with production of phenol, nitrogen, and hydrochloric acid—

$$C_6H_5.N_2.Cl + H_2O = C_6H_5.OH + N_2 + HCl.$$

If, therefore, we treat a warm solution of aniline chloride with nitrous acid, we obtain phenol, nitrogen, water, and hydrochloric acid, according to the equation—

$$C_6H_5.NH_3Cl + HNO_2 = C_6H_5.OH + N_2 + HCl + H_2O,$$

which is exactly comparable with the action of nitrous acid on the chloride of a primary fatty amine. The essential difference is that in the case of an aromatic amine, a diazo compound is produced as an intermediate product, whereas with the fatty amine no such compound is formed.

Phenyl-diazonium chloride when warmed with ethyl alcohol may react in either of two ways. The first reaction corresponds exactly to that with water, only that instead of phenol we obtain phenetole, the ethyl ether of phenol—

$$C_6H_5.N_2.Cl + C_2H_5OH = \underset{\text{Phenetole}}{C_6H_5.OC_2H_5} + N_2 + HCl.$$

In the second reaction, which occurs at the same time as the first, the alcohol acts as a reducing agent, being itself oxidised

to aldehyde. Here instead of phenol we obtain benzene, the diazo residue being replaced by hydrogen—

$$C_6H_5.N_2.Cl + C_2H_5OH = C_6H_6 + N_2 + HCl + C_2H_4O.$$

When phenyl-diazonium chloride is treated with a concentrated solution of potassium iodide, or when a solution of phenyl-diazonium iodide is warmed, nitrogen is evolved, and the iodine atom takes the place of the diazo group—

$$C_6H_5.N_2.I = \underset{\text{Iodobenzene}}{C_6H_5I} + N_2.$$

The diazo group can also be replaced by chlorine, bromine, or cyanogen by heating the diazonium salt with cuprous chloride, bromide, or cyanide (Sandmeyer's reaction). Apparently double salts of diazonium and cuprous copper are formed, which split very readily with elimination of nitrogen. A modification of this method is to use diazonium salts along with finely divided metallic copper, when the same reaction takes place—

$$\begin{aligned} C_6H_5.N_2.Cl &= C_6H_5.Cl + N_2 \\ C_6H_5.N_2.Br &= C_6H_5.Br + N_2 \\ C_6H_5.N_2.CN &= C_6H_5.CN + N_2 \end{aligned}$$

From the above it will be seen that formation and decomposition of diazo compounds are important processes for the substitution of one group for another in aromatic chemistry. Hydrogen in the nucleus of the original compound may be replaced by the nitro group NO_2, through the action of nitric acid ; this may then be reduced to the amino group NH_2, and then by diazotisation and subsequent decomposition of the diazo compound, which need seldom be separated from solution, we may replace the amino group by hydroxyl, a halogen, the cyanogen group, etc.

The diazo compounds not only decompose thus with elimination of nitrogen, they are also capable of entering readily into double decomposition with aromatic bases and phenols without loss of nitrogen. Instances of this type of reaction will be given later in connection with the production of azo dyes (p. 320).

Hydrazines.

Hydrazine proper is the nitrogenous base N_2H_4 prepared from guanidine (p. 234). Aromatic derivatives of it are easily formed by the reduction of diazonium salts. Thus, if phenyl-diazonium chloride is reduced by a solution of stannous chloride in hydrochloric acid, it is converted into phenyl-hydrazine chloride—

$$C_6H_5.N_2.Cl + 4HCl + 2SnCl_2 = C_6H_5.NH.NH_3Cl + 2SnCl_4$$

Phenyl-hydrazine, $C_6H_5NH.NH_2$.—The chloride of this substance may be prepared as above by reduction of the diazonium chloride with stannous chloride, but it is generally prepared by a somewhat different process. Benzene-diazonium chloride is treated with a solution of sodium sulphite, then reduced with sulphurous acid, and the resulting product heated with hydrochloric acid.

The chloride of phenyl-hydrazine so obtained may be decomposed by means of potash solution, the liberated base being then extracted by means of ether. After drying and evaporation of the ether, the base remains as an oily liquid which can be purified by distillation under diminished pressure.

Phenyl-hydrazine, when pure, is a colourless crystalline substance which melts at 23°. It is only sparingly soluble in water, but readily soluble in alcohol and in ether. It acts as a monacid base, and forms well-defined salts with the ordinary acids. Thus the chloride $C_6H_5NH.NH_3Cl$, formed by addition of hydrochloric acid, crystallises well from water, in which it is moderately soluble. It reduces Fehling's solution in the cold, yielding two atoms of hydrogen for reducing purposes and being converted into benzene and nitrogen—

$$C_6H_5.NH.NH_2 = C_6H_6 + N_2 + 2(H).$$

As we have seen, it is extensively used as a reagent for aldehydes and ketones, with which it forms phenyl-hydrazones; and from the point of view of physiological chemistry it is specially useful in the detection and discrimination of sugars on account of the double hydrazones or osazones which it forms with them. In this connection it should be noted that phenyl-

hydrazine acts as an oxidising agent (p. 194), the equation for its decomposition being—

$$C_6H_5.N.NH_2 + 3(H) = C_6H_5.NH_2 + NH_3.$$

It is manufactured chiefly as one of the substances required for the synthesis of the important drug antipyrine (p. 281).

Azo Compounds.

Azobenzene, $C_6H_5.N:N.C_6H_5$, is the parent substance of the azo compounds, many of which are of great importance as dyes. It may be prepared from nitrobenzene by first of all reducing this to **azoxybenzene** by means of sodium methoxide (which is oxidised to sodium formate), and then by heating the azoxybenzene so obtained with iron filings to remove the superfluous oxygen—

$$\underset{\text{Azoxybenzene}}{C_6H_5.\overset{\diagup\overset{O}{}\diagdown}{N—N}.C_6H_5} + Fe = \underset{\text{Azobenzene}}{C_6H_5.N:N.C_6H_5} + FeO.$$

Azobenzene forms brilliant red plates which are insoluble in water, but readily soluble in alcohol and ether. Though coloured, it is not itself a dye (p. 314).

ORGANIC ARSENIC COMPOUNDS.

It will be recalled that phosphorus and arsenic belong to the same natural family of elements as nitrogen. It might be expected, therefore, that we should have organic compounds of phosphorus and arsenic corresponding in a general way to those of nitrogen. This is to some extent the case. Thus, just as we derive primary, secondary, and tertiary amines from ammonia, NH_3, by replacing the nitrogen atoms by alkyl groups, so we can obtain from phosphine, PH_3, and arsine, AsH_3, by similarly replacing the hydrogen which they contain, primary, secondary, and tertiary phosphines and arsines. Such compounds are much less strongly basic than those of nitrogen; indeed, in the case of arsenic, basic properties are practically absent. Besides these compounds we have also oxidised compounds both of phosphorus and arsenic. The phosphorus derivatives are not used in medicine, but many of the organic compounds of arsenic are of great importance.

Cacodylic acid, $(CH_3)_2AsO.OH$.—When arsenic trioxide is distilled with potassium acetate, an oily liquid passes over which has very poisonous properties and an overpowering smell. The chief constituent of this oily liquid is a substance known as **cacodyl oxide**, $(CH_3)_2As.O.As(CH_3)_2$, the formation of which may be represented by the following equation:—

$$As_2O_3 + 4CH_3.COOK = \underset{\text{Cacodyl oxide}}{(CH_3)_2As.O.As(CH_3)_2} + 2K_2CO_3 + 2CO_2.$$

This substance contains the radical cacodyl $As(CH_3)_2$, which formally corresponds to the dimethyl-amino group $N(CH_3)_2$. Besides cacodyl oxide, the liquid also contains **cacodyl**, formed by the union of two of the cacodyl groups as follows—

$(CH_3)_2As . As(CH_3)_2$. This compound is spontaneously inflammable, and corresponds in the nitrogen series to tetramethylhydrazine, $(CH_3)_2N . N(CH_3)_2$. When cacodyl oxide is treated with hydrochloric acid it is converted into cacodyl chloride, according to the following equation:—

$$(Me_2As)_2O + 2HCl = 2Me_2AsCl + H_2O.$$

Here we see a difference between the corresponding compounds of nitrogen and arsenic which is also apparent in the inorganic compounds of these elements. Nitrogen, when triad, has little tendency to combine with chlorine; arsenic, on the other hand, readily forms a chloride, and here we see that a chloride of a triad arsenical radical can be easily obtained.

If the oily mixture containing cacodyl and cacodyl oxide is oxidised, both of these substances are converted into **cacodylic acid**, or dimethyl-arsinic acid, $(CH_3)_2AsO . OH$, the salts of which are used in medicine. It is a crystalline acid which is readily soluble in water and in alcohol. The sodium salt $(CH_3)_2AsO . ONa, 3H_2O$ is that which is most commonly employed. It is a white crystalline powder readily soluble in water. Cacodylic acid and its salts are much less poisonous than arsenious acid and the salts derived from it, so that they may be administered in much larger doses.

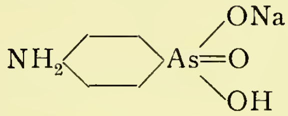
Arrhenal, *sodium methyl-arsonate*, $CH_3 . AsO(ONa)_2$, is prepared by the action of methyl iodide on sodium arsenate in presence of excess of alkali—

$$O{=}As\begin{cases}ONa\\ONa\\ONa\end{cases} + CH_3I = O{=}As\begin{cases}CH_3\\ONa\\ONa\end{cases} + NaIO.$$

The sodium hypo-iodite represented as being here formed enters into further decompositions. Arrhenal is very soluble in water, and is used medicinally for the same purposes as sodium cacodylate.

These arsenical compounds containing fatty radicals are somewhat too stable in the body to produce the desired arsenical effect, and their place has been largely taken in recent years by compounds containing aromatic radicals.

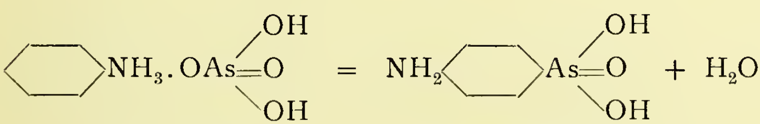
Atoxyl, *sodium* p-*amino-phenyl-arsonate.*—This substance has the graphic formula—



Atoxyl

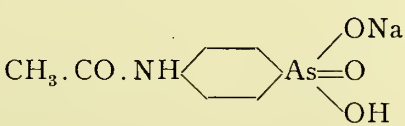
It corresponds to arrhenal, except that for the methyl group the *p*-amino-phenyl group has been substituted. The presence of the amino group in the aromatic part neutralises one of the acidic hydroxyl groups in the arsenical part of the molecule, so that the sodium compound has only one sodium atom instead of the two found in arrhenal.

Atoxyl is prepared by heating aniline and arsenic acid together at a temperature of 190°. Aniline arsenate is first formed, and then transformed at this temperature with loss of water into *p*-amino-phenyl-arsonic acid, which may be purified by crystallisation, and converted into the sodium salt by neutralisation with sodium hydroxide—



Aniline arsenate   *p*-Amino-phenyl-arsonic acid

The sodium salt may then be recrystallised from rectified spirit. Arsenic in this form may be administered in comparatively large doses in the treatment of certain skin diseases, malaria, sleeping sickness, etc. The corresponding mercuric salt is also used. The acetyl derivative

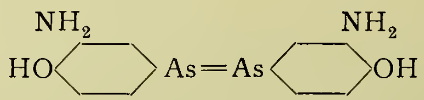


Acetyl-atoxyl

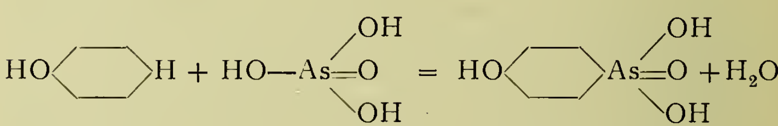
is likewise employed under the name **arsacetin.**

The above arsenical compounds all contain arsenic in the pentad state. Some valuable therapeutic agents are prepared by the reduction of aromatic pentad arsenical compounds into those in which the arsenic is triad.

***p*-Dihydroxy-*m*-diamino-arseno-benzene.** — This substance has the constitutional formula—

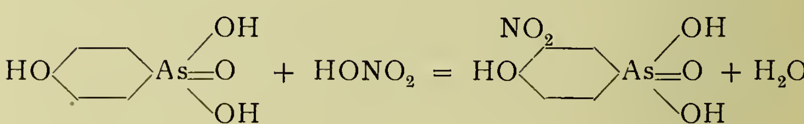


p-Hydroxy-phenyl-arsonic acid is prepared by heating phenol and arsenic acid—

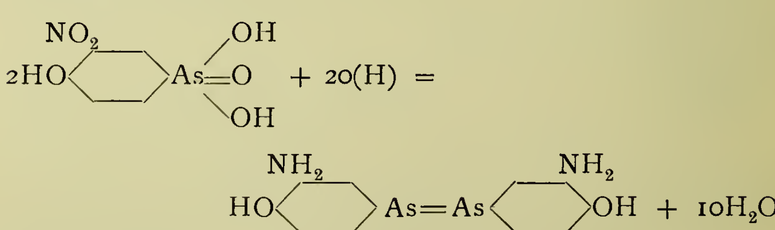


Phenol   Arsenic acid   *p*-Phenol-arsonic acid

It is then nitrated by means of a mixture of nitric acid and sulphuric acid—

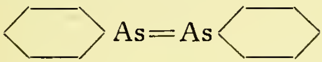


On reduction with sodium hydrosulphite in presence of alkali, the nitro group is not only converted into the amino group, but the arsenic is completely deoxidised, and the two residues unite together as follows :—

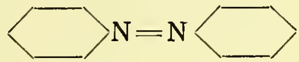


It will be noticed that the formulation of this arseno compound

closely corresponds to that of an azo compound, arseno-benzene having a formula comparable with that of azobenzene—



Arseno-benzene

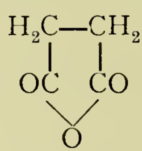


Azobenzene

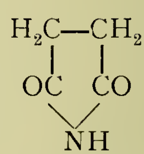
The base is diacid, and the chloride $[AsC_6H_3(OH)(NH_2)]_2,2HCl$ is the compound which is sold under the trade name of **salvarsan.**

HETEROCYCLIC COMPOUNDS.

The benzene ring and the cyclohexane ring are termed homocyclic, because each member in the closed chain contains the same element, carbon. A great many rings, however, exist in which the members linked up together contain different elements. Such rings are called heterocyclic rings. We have already, in a way, had examples of such rings in substances like succinic anhydride and succinimide—



Succinic anhydride



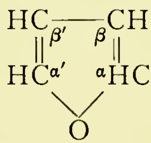
Succinimide

These are ring structures, each chain containing four carbon links, together with one oxygen link in succinic anhydride, and one nitrogen link in succinimide. Such substances, however, are not classed with heterocyclic compounds in the ordinary sense in which the term is used. The rings in them are too easily split, and we generally understand by heterocyclic compounds, compounds in which the rings are not easily opened by the action of ordinary reagents, and from which many derivatives can be obtained with the ring structure unimpaired.

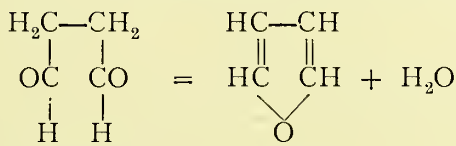
Heterocyclic rings containing one or more nitrogen links are by far the most important, but one or two heterocyclic compounds containing no nitrogen in the ring require mention.

FURANE GROUP.

Furane, C_4H_4O.—The graphic formula of this substance is—

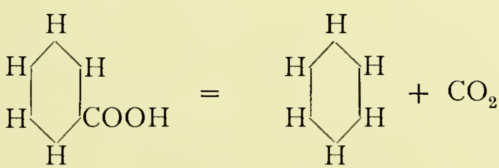


It may be derived from succinic aldehyde by removal of water—

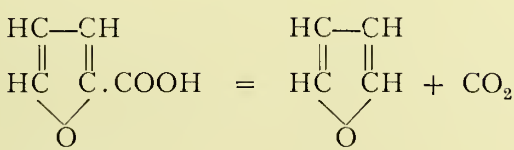


Succinaldehyde Furane

Here a closed chain is formed from an open chain with elimination of water, a process corresponding to the production of succinic anhydride from succinic acid. Furane is most easily prepared by heating a salt of pyromucic acid with soda-lime, the action being precisely analogous to the preparation of benzene from benzoic acid—



Benzoic acid Benzene



Pyromucic acid Furane

Furane is a colourless liquid which boils at 32°, and is insoluble in water. The position of substituting groups in the molecule is indicated by means of the Greek letters to be seen in the graphic formula, which shows that there are two species of mono-derivatives, α and β.

Furfural, *pyromucic aldehyde,* α-$C_4H_3O.CO.H$.—This aldehyde is very simply formed by distilling pentoses with hydrochloric acid or with dilute sulphuric acid. The action which takes place is as follows (p. 201):—

$$C_5H_{10}O_5 = C_4H_3O.CO.H + 3H_2O.$$

Here we have another example of the formation of a closed chain from an open chain by removal of water. Furfural passes over with the steam, and condenses as a colourless oil, which boils at 162°. In its properties it exactly resembles benzoic aldehyde, and differs from the fatty aldehydes. Thus, with concentrated potash it is converted partly into a primary alcohol and partly into pyromucic acid, as benzoic aldehyde under the same treatment is converted into benzyl alcohol and benzoic acid. It may easily be distinguished from benzaldehyde, inasmuch as it gives a bright red colour on treatment with a salt of aniline.

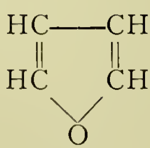
Pyromucic acid, α-$C_4H_3O.COOH$.—This substance is prepared by oxidation of furfural, and also by the dry distillation of mucic acid, $C_6H_{10}O_8$ (p. 196), under reduced pressure—

$$C_6H_{10}O_8 = C_4H_3O.COOH + CO_2 + 3H_2O.$$

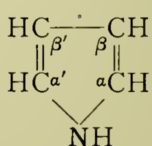
It is a solid which melts at 134°, and resembles benzoic acid closely in its behaviour. Like the latter, it sublimes readily, is freely soluble in boiling water but sparingly soluble in cold water.

PYRROLE GROUP.

Pyrrole has a formula closely resembling that of furane, the difference being that instead of the dyad oxygen atom of the furane ring, the pyrrole ring contains a dyad nitrogen group, NH. The relationship is evident on considering their graphic formulæ—

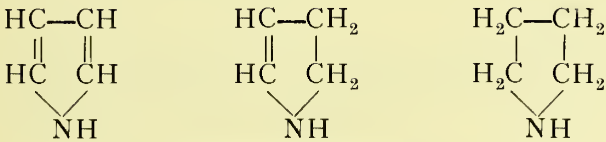


Furane



Pyrrole

If pyrrole, C_4H_5N, is reduced by means of zinc and acetic acid, it takes up two atoms of hydrogen and forms another ring compound, C_4H_7N, named **pyrroline**, which, when reduced further with sodium and alcohol, takes up two more hydrogen atoms and becomes the substance **pyrrolidine**, C_4H_9N. The following formulæ show how these rings are related to each other—



Pyrrole   Pyrroline   Pyrrolidine

These rings are important from the point of view of medical chemistry.

Pyrrole, C_4H_5N.—When bones are subjected to destructive distillation for the purpose of producing bone charcoal, a liquid distillate known as **bone oil** or bone tar is obtained. The portion of this which on redistillation boils between 100° and 150° contains pyrrole, which may be separated from the other substances with which it is mixed first by treatment with dilute sulphuric acid to remove stronger bases in the form of salts. Pyrrole itself is an excessively weak base, and only very little soluble even in acid solutions. The separated pyrrole is then warmed with excess of caustic potash solution to remove acids, and again distilled. The fraction passing over in the neighbourhood of 130° is heated with solid caustic potash. We have seen that in succinimide and similar compounds, the hydrogen of the imino group NH is replaceable by metal. This replacement takes place in the case of pyrrole, so that when heated with solid potash it is converted into potassium pyrrole, C_4H_4NK, which is also a solid. The other substances in the oil are not acted upon by potassium hydroxide, and since they remain liquid may be easily separated from the potassium pyrrole, which is then decomposed by means of water—

$$\underset{\text{Potassium pyrrole}}{C_4H_4NK} + H_2O = \underset{\text{Pyrrole}}{C_4H_4NH} + KOH.$$

The liberated pyrrole is distilled over with steam and purified by further fractional distillation.

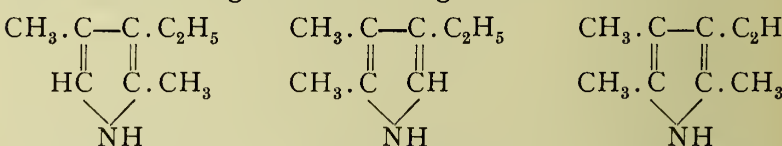
Pyrrole is a colourless liquid which turns brown in air and has a smell resembling that of chloroform. It boils at 130°, and possesses a specific gravity slightly less than that of water. It is very sparingly soluble in water, but mixes readily with alcohol and ether. It and many of its volatile derivatives may be readily recognised by the property which they possess of turning a splinter of pine wood moistened with hydrochloric acid intensely red.

Pyrrole has a decidedly aromatic character, but behaves more like the aromatic base aniline than like benzene itself. Owing to its slightly acidic character it also resembles phenol.

Hæmoglobin and Chlorophyll.

Chlorophyll (through the medium of which carbon dioxide is absorbed by plants, with ultimate liberation of oxygen) and hæmoglobin (through the medium of which oxygen is absorbed by animals, with ultimate liberation of carbon dioxide) are from the chemical standpoint closely related substances.

Hæmoglobin may be split up by acid hydrolysis into a protein, *globin*, and a red colouring matter, *hæmatin*. **Chlorophyll** by mild alkaline hydrolysis may be decomposed into methyl alcohol, the unsaturated alcohol *phytol*, $C_{20}H_{39}OH$, and *chlorophyllin*, which is the analogue of hæmatin. Hæmatin and chlorophyllin are still very complex substances, but both yield on further hydrolysis and reduction alkyl-pyrroles, amongst which the following have been recognised :—



Hæmopyrrole Isohæmopyrrole Phyllopyrrole

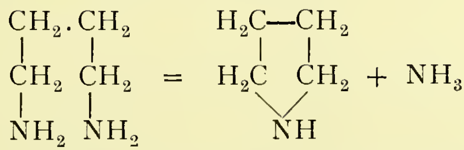
It may be noted that whereas iron is a constant metallic constituent of hæmoglobin, magnesium is a constant metallic constituent of chlorophyll. The following empirical formulæ give the composition of the two substances as far as they are known at present :—

Hæmatin . .	$C_{34}H_{32}N_4O_5Fe$
Chlorophyllin . .	$C_{34}H_{32}N_4O_6Mg$

Pyrrolidine, C_4H_9N.

This ring occurs in many alkaloids, so that derivatives of it are found amongst the decomposition products of the complex alkaloid molecules. Derivatives of pyrrolidine likewise go to build up some of the complex proteins, so that both from the point of view of pharmacological and physiological chemistry this ring is of great interest.

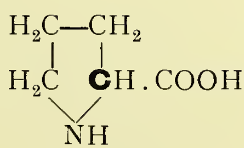
Pyrrolidine itself may, as has been stated, be prepared by the reduction of pyrrole. It may also be prepared by heating the chloride of tetramethylene-diamine—



It is a liquid which boils at 87°, and mixes with water in all proportions, yielding a strongly alkaline solution with a penetrating ammoniacal smell. In this respect pyrrolidine differs entirely from pyrrole, which as we have seen is sparingly soluble in water, and is possessed of very feeble basic properties.

One may see in general that pyrrole behaves like an aromatic substance, whereas the reduced pyrroles such as pyrrolidine behave like fatty substances. This corresponds to what we have seen in the homocyclic chains; benzene is the typical aromatic hydrocarbon, whereas its reduction product cyclohexane, C_6H_{12}, is practically without aromatic properties, it and its derivatives being of distinctly aliphatic character.

Proline, *α-pyrrolidine-carboxylic acid.*—The graphic formula of this substance is—



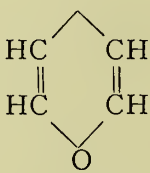
It may be obtained by the hydrolysis of many proteins, and was first prepared by the hydrolysis of casein from milk by means of hydrochloric acid. It has also been prepared synthetically. It

is a solid substance which melts at 205°. Its aqueous solution is faintly acid to litmus, and has a sweet taste. Since the carbon atom to which the carboxyl group is attached is asymmetric, a dextro and a lævo variety of the acid are possible together with the inactive racemic mixture of the two. The acid derived from casein is partly this racemic mixture and partly the lævo variety.

Hydroxy-proline is also found amongst the products of the hydrolysis of proteins. The position of the hydroxyl group in the molecule is not known with certainty. It is probably, however, on the carbon atom adjacent to that bearing the carboxyl group.

PYRONE GROUP.

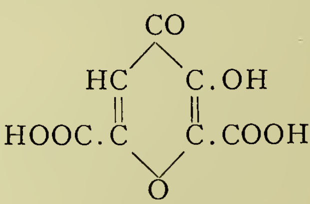
A γ-pyrone ring consists of an oxygen link and five carbon links, one of which is oxidised, the oxidised carbon being in the γ-position with regard to the oxygen atom—



γ-Pyrone

This ring is found in many natural substances.

Meconic acid occurs in opium, where it is united with the opium alkaloids to form salts. It is a pyrone dicarboxylic acid of the formula—



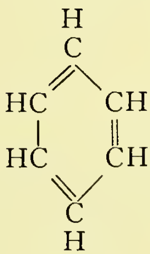
Meconic acid

The acid is a colourless crystalline solid, moderately soluble in water. Its solutions give with ferric chloride a red coloration,

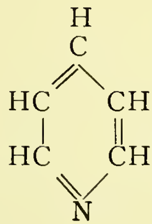
which (unlike the similar coloration given by thiocyanates) is not discharged on addition of mercuric chloride.

PYRIDINE GROUP.

The formula of pyridine resembles that of benzene, with this difference, that one of the CH groups in the benzene ring is replaced by a nitrogen atom—

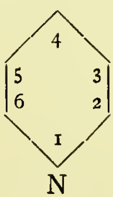


Benzene

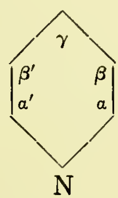


Pyridine

The above formula for pyridine corresponds to Kekulé's formula for benzene, but it is possible to write a centric formula for pyridine analogous to that given for benzene. The position of substituting groups for the hydrogens of pyridine is indicated either by means of numbers attached to the ring or by Greek letters as follows :—



or



An inspection of the formula shows that there may be three mono-substitution products in the case of pyridine, whilst there is only one in the case of benzene.

Pyridine, C_5H_5N, is a product of the destructive distillation of many nitrogenous organic substances. Thus it is formed when certain alkaloids are heated, and also on a large scale in the distillation of coal, wood, and bones. It is therefore found along with hydrocarbons in coal-tar and in bone-oil. From these liquids it may be separated along with other basic substances by means of sulphuric acid, which forms soluble salts

with the bases. The aqueous solutions of sulphates thus obtained yield the bases again in the form of oil when excess of alkali is added. When the oil is subjected to fractional distillation pyridine is obtained in the lowest boiling fractions. It may be prepared in the pure state by heating nicotinic acid, $C_5H_4N . COOH$, with soda-lime. The action is analogous to the production benzene from benzoic acid.

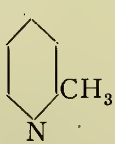
Pyridine is a colourless liquid with a characteristic odour. It boils at 114°, and has a specific gravity slightly greater than that of water, with which it mixes in all proportions. It is also freely soluble in alcohol and in ether.

In its chemical behaviour pyridine is a tertiary base. It is of much the same strength as aniline, and unites with acids to form salts. Thus we have pyridine chloride, C_5H_5NHCl, pyridine sulphate, $(C_5H_5N)_2H_2SO_4$, etc. Like other tertiary bases it unites readily with the methyl iodide to form the iodide of a quaternary base—

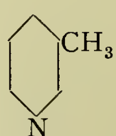
$$C_5H_5N + CH_3I = \underset{\text{Pyridine methyl iodide}}{C_5H_5NCH_3{}'I'}.$$

The pyridine ring is extremely stable. It is not attacked by chromic acid or nitric acid. The halogens yield addition compounds easily, but substitution products only with difficulty. Sulphuric acid at about 300° acts with production of a sulphonic acid. Pyridine thus differs somewhat from both fatty and aromatic compounds, but its derivatives show a general similarity to the benzene compounds, and are thus generally classified along with the aromatic substances.

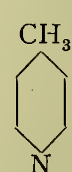
Mono-derivatives of Pyridine.—Along with pyridine in the basic oil there occur homologues of pyridine, the hydrogen in the pyridine ring being replaced by one or more methyl groups. Amongst these homologues may be mentioned the three isomeric monomethyl pyridines, or **picolines**, the formulæ of which are given below—



α-Picoline

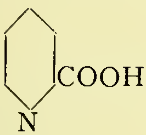


β-Picoline

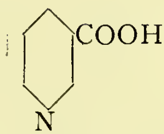


γ-Picoline

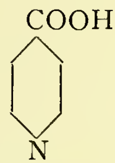
These picolines resemble pyridine closely in their properties. They are readily attacked, however, by potassium permanganate or nitric acid, when they behave like toluene, the corresponding benzene derivative, the methyl group being converted by the oxidising agent into the carboxyl group. The three monobasic acids thus resulting from the three isomeric picolines have the names and formulæ given below—



Picolinic acid



Nicotinic acid

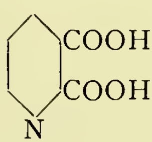


Isonicotinic acid

These acids are amphoteric, like glycine, and form salts both with acids and with bases. The β acid, or nicotinic acid, may also be produced by the oxidation of the alkaloid nicotine. When any of these acids is heated with excess of soda-lime it decomposes with loss of carbon dioxide and formation of pyridine—

$$\underset{\text{Sodium nicotinate, etc.}}{C_5H_4N.COONa} + NaOH = \underset{\text{Pyridine}}{C_5H_5N} + Na_2CO_3.$$

Di-derivatives of Pyridine.—There are six different dimethyl pyridines or **lutidines**, and these, when oxidised, yield six isomeric dicarboxylic acids. The only one of these which need be noted is that known as **quinolinic acid**, the formula of which is—

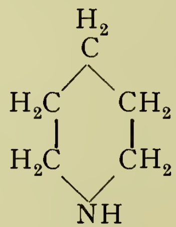


Quinolinic acid

This substance is produced by the oxidation of the base quinoline by means of potassium permanganate. When heated carefully to about 200°, it decomposes into carbon dioxide and nicotinic acid. This behaviour may be contrasted with that of the corresponding benzene derivative, phthalic acid, which on heating does not lose carbon dioxide, but water, with formation of phthalic anhydride.

Piperidine.

This substance is hexahydro-pyridine, $C_5H_{10}NH$, and bears the same relationship to pyridine as cyclohexane does to benzene. Its graphic formula is given below—



Piperidine

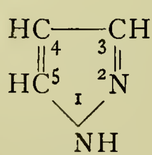
It may be formed from pyridine by direct reduction with sodium and alcohol—

$$C_5H_5N + 6(H) = C_5H_{10}NH.$$

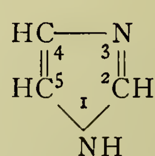
It may also be produced by decomposing the alkali piperine found in pepper with caustic potash, or by distilling the chloride of pentamethylene diamine (p. 239). It is a colourless liquid with a peculiar ammoniacal odour. It boils at 105°, and mixes with water, alcohol, and ether in all proportions. It behaves chemically like a fatty secondary base, differing in this respect from pyridine, which behaves as a tertiary aromatic base. Piperidine is much more strongly basic than pyridine.

HETEROCYCLIC RINGS CONTAINING TWO NITROGEN LINKS.

The following heterocyclic rings of five links, containing two nitrogen atoms, may be noted :—



Pyrazole



Imidazole or Glyoxaline

These rings are derived from pyrrole by the substitution of

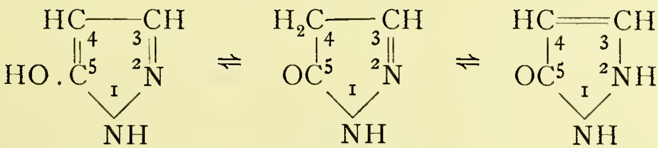
triad nitrogen for the triad group CH in the 2 and 3 position respectively.

PYRAZOLE GROUP.

Pyrazole, $C_3H_4N_2$, is a distinctly aromatic substance in its behaviour. It is a crystalline solid, and is a well-defined base which forms definite salts with acids, in this respect differing from pyrrole and resembling pyridine. It may be chlorinated, sulphonated, and nitrated in much the same way as benzene, and it is possible to reduce the nitro substances to amino substances, and from these to derive diazo compounds quite analogous in their properties to those formed from benzene.

5-Hydroxypyrazole, generally known as **5-pyrazolone**, has distinctly phenolic characters. It may exist in three tautomeric forms, the formulæ for which are given below—

I. II. III.



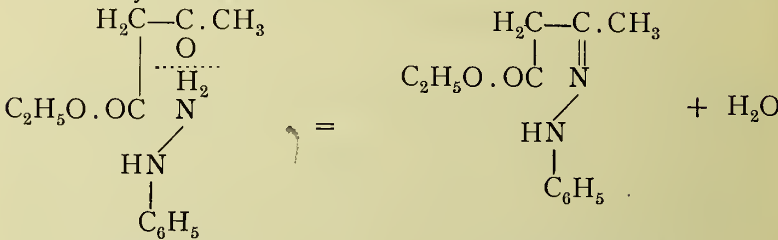
5-Pyrazolone

The ketonic termination *-one* indicates the presence of the CO group in II. and III. A hydrogen atom is mobile, and leaves its original place in order to enter a new union with an atom next but one to that with which it was originally bound. Thus in I. the hydrogen of the hydroxyl group leaves the oxygen, passes over the carbon atom 5, and lands on the unsaturated carbon atom 4. In this way formula II. is obtained. The mobile hydrogen atom, however, may still further transfer itself from 4 by passing over the carbon atom 3 to the unsaturated nitrogen atom 2, giving rise to the formula III. Derivatives of all three forms are known.

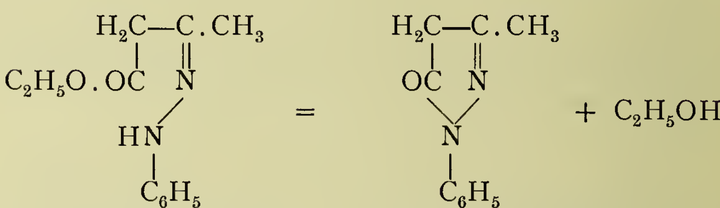
Antipyrine, *phenazone*, 1-*phenyl*-2,3-*dimethyl*-5-*pyrazolone*.—This substance is the most important derivative of pyrazole, and is manufactured on a large scale for use in medicine as a febrifuge. 1-Phenyl-3-methyl-5-pyrazolone is first produced by heating together acetyl-acetic ester, $CH_3 . CO . CH_2 . COOC_2H_5$, and phenyl-hydrazine, $NH_2 . NHC_6H_5$. This substance is then

methylated by heating with methyl iodide. The various actions are shown by the following formulæ:—

Acetyl acetic ester

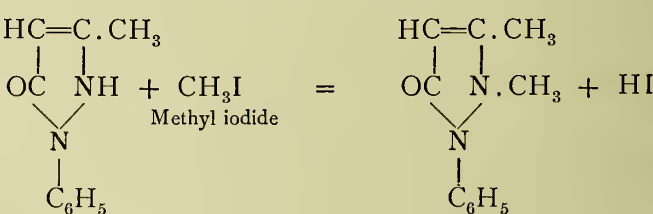


Phenyl-hydrazine — Phenyl-hydrazone of ester



Phenyl-hydrazone of ester — Phenyl-methyl-pyrazolone

The formula of the phenyl-methyl-pyrazolone is that corresponding to II. above, but when heated with methyl iodide the substance acts as if it possessed a formula corresponding to III., so that we have the action—

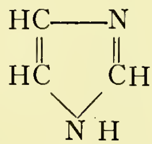


Phenyl-methyl-pyrazolone — Antipyrine

Antipyrine is a white crystalline substance melting at 113°, and easily soluble in water and in alcohol. It is a mon-acid base, and forms stable salts. The salicylate is used in medicine under the name of **salipyrine.**

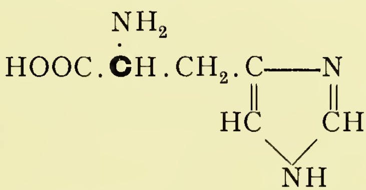
IMIDAZOLE GROUP.

Imidazole, *glyoxaline*, is isomeric with pyrazole, the nitrogen atoms not being neighboured in the ring but separated by a carbon atom—



It may be formed from glyoxal, H . CO . CO . H, and ammonia, whence the name glyoxaline. It is a solid which melts about 90°, and is a stronger base than pyrazole. The imidazole ring occurs in many natural substances—*e.g.*, in the alkaloids from jaborandi.

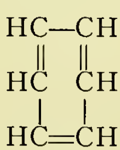
Histidine is a derivative of imidazole, and has the formula—



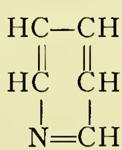
It is a frequent product of the hydrolysis of proteins.

PYRIMIDINE GROUP.

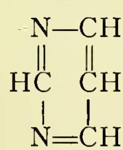
Pyrimidine, $C_4H_4N_2$, may be regarded as pyridine, in which a CH group in the meta position to the nitrogen atom has been replaced by a second nitrogen atom. It therefore bears the same relation to pyridine as pyridine does to benzene—



Benzene



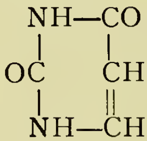
Pyridine

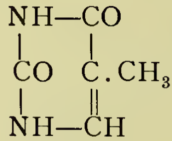


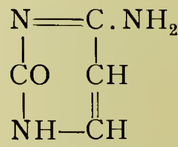
Pyrimidine

Several oxidised derivatives of pyrimidine are of physiological

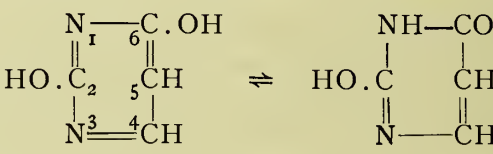
importance, as being products of the breaking up of the nucleins. These are—


Uracil
2,6-Dioxypyrimidine


Thymine
5-Methyl-uracil


Cytosine
6-Amino-2-oxypyrimidine

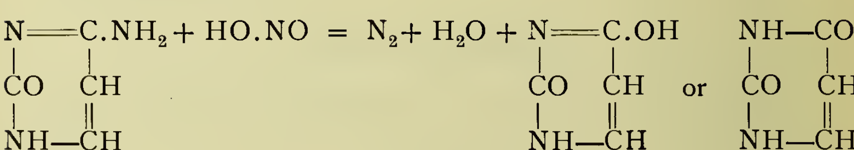
2,6-Dihydroxypyrimidine has the formula I. below—


I. II.

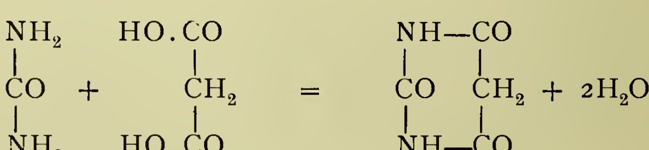
Tautomerism of the type already encountered with the pyrazolone group leads to formula II., and if it further occurs at the group 2,3, we obtain the formula of uracil given above.

Pyrimidine itself is a more powerful base than pyridine. Its oxy-derivatives are much less basic, and exhibit incipient acidic (phenolic) properties as well.

If the amino-derivative **cytosine** is treated with nitrous acid, the usual replacement of NH_2 by OH occurs, with production of uracil—

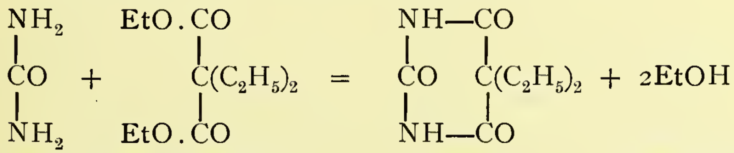

Cytosine Uracil

Barbituric acid is prepared by heating together malonic acid and urea—


Urea Malonic acid Barbituric acid

It may be conceived as trioxy-pyrimidine, for on chlorination with phosphorus oxychloride and subsequent reduction it yields pyrimidine. Although it contains no carboxyl group it has distinct acid properties, acting as a feeble monobasic acid.

Veronal, *diethyl-barbituric acid,* is prepared by the action of urea on the ethyl ester of diethyl-malonic acid (p. 131)—

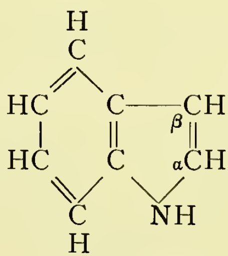


Urea Diethyl-malonic ester Veronal Ethyl alcohol

Like barbituric acid, veronal possesses acid properties, and both it and its sodium salt, which is somewhat more soluble, are used in medicine as hypnotics. Veronal is a white crystalline substance melting at 191°, and is soluble in about 150 parts of water.

INDOLE GROUP.

Indole, C_8H_7N, has a constitution expressed by the following formula :—

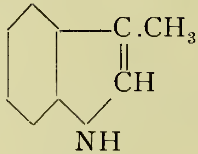


Indole

It is composed of a benzene ring and a pyrrole ring, with two carbon atoms in common. It is formed in small quantity in the putrefaction of proteins, and is also contained in the oil from jasmine blossoms. When impure it has an unpleasant fæcal smell, but when perfectly pure it imparts a freshness to the odour of other perfumes. It is a solid which melts at 52°, and resembles pyrrole in its chemical properties.

Many of its derivatives are of physiological interest, and the important dye indigo is derived from it.

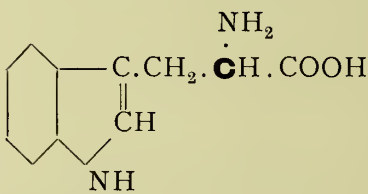
Skatole, C_9H_9N, is β-methyl-indole—



Skatole

It is produced in the putrefactive decomposition of proteins, and is found in human fæces; it possesses an extremely offensive odour.

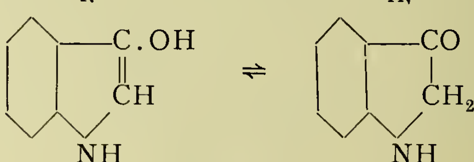
Tryptophane is a product of the hydrolysis of many proteins, and from it both indole and skatole are produced in putrefactive processes. It is β-indole-α-amino-propionic acid, and has the formula—



Tryptophane

Indoxyl, C_8H_7NO, is β-hydroxy-indole, and its formula may be written in either of the two following tautomeric forms:—

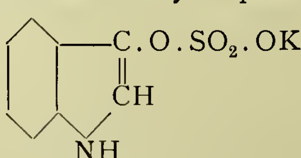
I. II.



Indoxyl

When the glucoside indican contained in indigo-producing plants is hydrolysed it yields glucose and indoxyl (p. 212).

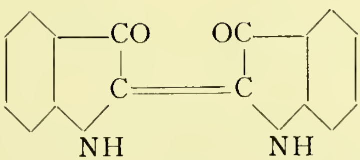
Urinary indican, which is found in the urine of man, and of herbivora, is potassium indoxyl sulphate—



Urinary indican

When this is hydrolysed by acids it breaks up into sulphuric acid and indoxyl. Since indoxyl is easily oxidised to indigo-blue, indican in the urine may be tested for by addition of concentrated hydrochloric acid, and a few drops of an oxidising agent such as hypochlorite solution or ferric chloride. The blue colour may be dissolved out by chloroform.

Indigotin, $C_{16}H_{10}O_2N_2$, or *indigo-blue*, has the constitutional formula—

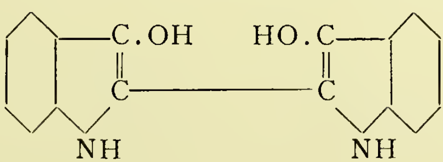


Indigotin

which is derived from formula II. of indoxyl by abstraction of hydrogen, which can be effected practically by means of an oxidising agent—

$$2C_8H_7ON + 2(O) = 2H_2O + C_{16}H_{10}O_2N_2.$$

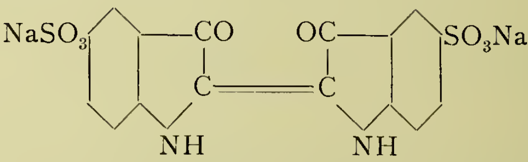
It is the chief constituent of commercial indigo, and is formed by the hydrolysis and atmospheric oxidation of the glucoside indican under the influence of enzymes present in the plant. It may be obtained by sublimation in crystals of copper-red metallic lustre. It is insoluble in water, alcohol, ether, alkalies, and dilute acids. By reduction with alkaline solution of sodium hydrosulphite it is converted into a colourless solution of **indigo-white,** which has two more hydrogen atoms in the molecule—



This substance being of a phenolic nature, dissolves readily in alkalies. An alkaline solution of indigo-white is used in dyeing, the material being soaked in it and then exposed to the air. Oxidation by atmospheric oxygen then occurs, and the indigo-

white is oxidised to insoluble indigo-blue (indigotin) in the fibre itself.

Indigo-carmine is the sodium salt of indigotin-disulphonic acid—

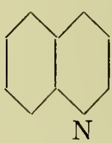


It is soluble in water, and is used as an acid dye in dyeing wool with indigo.

The ordinary "indigo solution" of the laboratory is prepared by dissolving indigo in concentrated sulphuric acid, when a soluble sulphonic acid is produced, and diluting with water.

QUINOLINE AND ISOQUINOLINE.

Quinoline and isoquinoline have the empirical formula C_9H_7N, and bear the same relationship to naphthalene as pyridine does to benzene. Their graphic formulæ may be written as follows, no attempt being made to indicate the position of the extra valencies:—



Quinoline

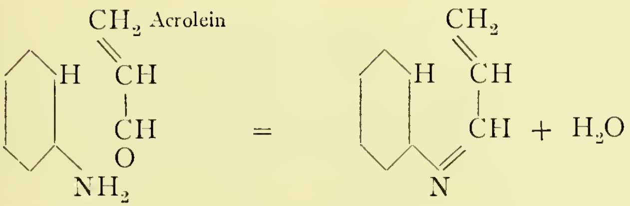
Isoquinoline

It will be seen that the molecule consists of two parts, namely, a benzene and a pyridine ring joined together, with two carbon atoms common to both rings. These carbon atoms are in the ortho- position with regard to each other.

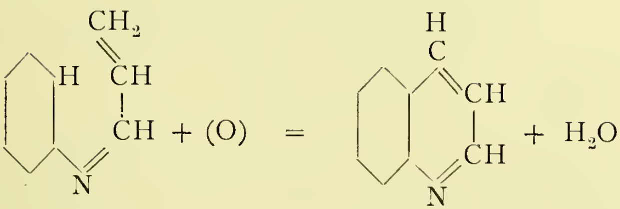
Quinoline and isoquinoline both occur in coal-tar and in bone oil. They are extracted along with the pyridine bases by the action of sulphuric acid, and are recovered from the sulphates on addition of alkali. They may also be obtained by heating certain alkaloids with caustic alkali. Generally, however, they are prepared synthetically.

Quinoline, C_9H_7N, may be prepared by heating together aniline, glycerol, and sulphuric acid, with nitrobenzene as oxidising agent. The action of sulphuric acid on glycerine produces acrolein (p. 115), which then reacts as an aldehyde with aniline to form acrolein-aniline. This on oxidation by nitrobenzene loses two hydrogen atoms; a new ring is formed, and quinoline results. These reactions may be expressed by means of the following equations:—

$$CH_2OH.CHOH.CH_2OH = \underset{\text{Acrolein}}{CH_2:CH.CO.H} + 2H_2O.$$



Aniline Acrolein-aniline

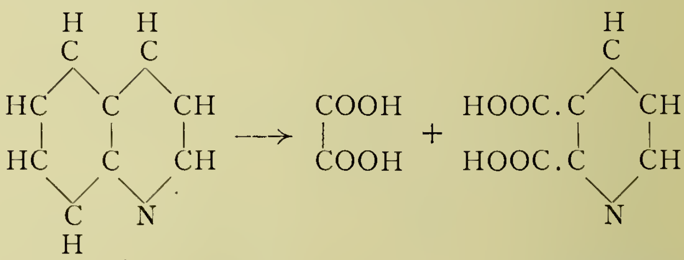


Acrolein-aniline Quinoline

The quinoline is liberated from the sulphate obtained in the above process by means of caustic soda, and is finally purified by fractional distillation.

Quinoline is a colourless, oily, and highly refractive liquid. It has a characteristic, not unpleasant, odour. It is very sparingly soluble in water, in which it sinks. It is soluble in most organic solvents. Like pyridine, it acts as a tertiary base, forming well-defined salts with the ordinary acids. These salts are generally soluble in water, the bichromate being the chief exception. Quinoline is a constituent of the cinchona alkaloids such as quinine.

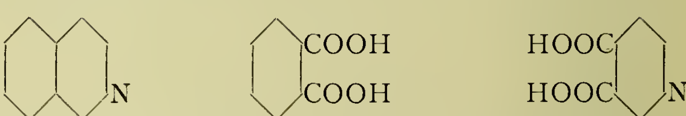
When quinoline is oxidised, the benzene ring is broken up, oxalic acid and quinolinic acid being produced (p. 279)—



Quinolinic acid

Isoquinoline occurs in coal-tar in smaller quantity than quinoline, from which it can be separated owing to the sparing solubility of its sulphate. At the ordinary temperature it is a solid which melts at 23°. In its other properties it closely resembles quinoline, and is important as a constituent of narcotin and other vegetable alkaloids.

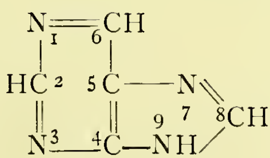
If it is oxidised, both the benzene and the pyridine ring are attacked. When the benzene ring is broken up, the resulting substance is cinchomeronic acid, or β-γ-pyridine-dicarboxylic acid; when the pyridine ring is broken up phthalic acid is produced, thus—



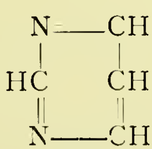
Isoquinoline yields Phthalic acid and Cinchomeronic acid

PURINE DERIVATIVES.

The substance purine itself is of little importance, but many of its derivatives are of great interest in animal and plant chemistry. The graphic formula of purine is—

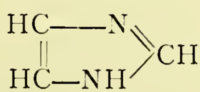


In this formula we have two rings joined together by means of neighbouring carbon atoms common to both (as in naphthalene, quinoline, etc.). These two rings are—



Pyrimidine

and

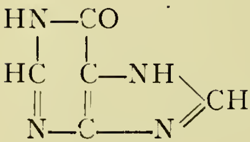


Pyrazole

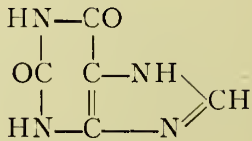
The atoms constituting the rings are numbered as in the graphic formula, in order to indicate the place of substituting atoms or radicals. The oxidised derivatives are of special importance, the oxidation being that of the carbon atoms in the 2, 6, 8 positions.

The following formulæ indicate the chief derivatives and their relationship to purine:—

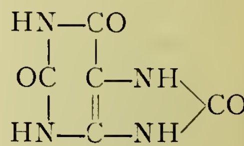
Oxypurines.



Hypoxanthine
6-Oxypurine

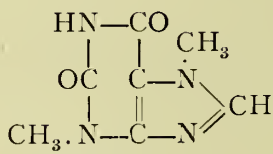


Xanthine
2,6-Dioxypurine

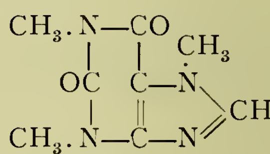


Uric acid
2,6,8-Trioxypurine

Methyl-xanthines.

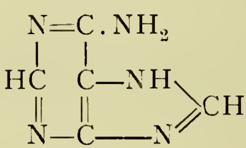


Theobromine
3,7-Dimethyl-xanthine

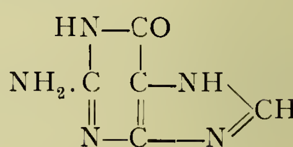


Caffeine
1,3,7-Trimethyl-xanthine

Amino-derivatives.



Adenine
6-Aminopurine

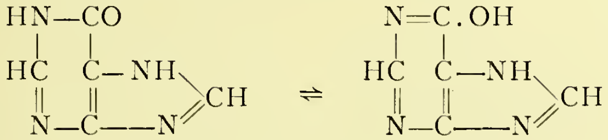


Guanine
2-Aminohypoxanthine

Hypoxanthine, $C_5H_4N_4O$, is found along with xanthine, guanine, and adenine as a hydrolysis product of the nucleins, which are nitrogenous bodies occurring in the cell nuclei. It can be prepared from meat extract, and when pure forms microscopic crystals which are moderately soluble in boiling water. It is an amphoteric substance, combining both with acids and with bases.

Hypoxanthine, like all the oxypurines, exhibits the phenomenon of tautomerism, and its formula may be written

in either of the two following ways, so that it may be regarded either as an oxy- or a hydroxy-derivative of purine :—



The basic properties of hypoxanthine are due to the presence of the NH groups; the seat of the acidic properties is more difficult to determine. The replaceable hydrogen may in the one formulation be a part of the imino group, or, in the other, of the group C.OH.

Xanthine, $C_5H_4N_4O_2$, is found in all the tissues of the body, and also to a small extent in urine. It is a colourless substance which is very sparingly soluble in water but easily soluble in caustic alkalies, from solutions in which it is reprecipitated on addition of acid. It is considerably less basic and more acid than hypoxanthine, the difference being no doubt due to the presence of a second oxygen atom.

Theobromine, 3,7-*dimethyl-xanthine*, $C_7H_8N_4O_2$, is contained in cocoa-nibs, and can be prepared from ordinary cocoa, which contains it to the amount of 1 to 2 per cent. It is a white crystalline powder, sparingly soluble in water, and possesses both acid and basic properties. Its silver salt when treated with methyl iodide yields trimethyl-xanthine, or caffeine—

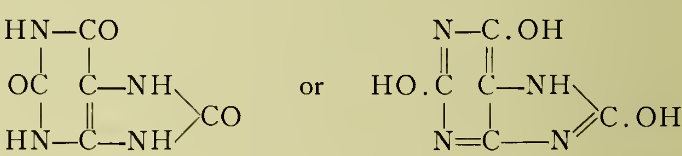
$$C_5HN_4O_2(CH_3)_2Ag + CH_3I = C_5HN_4O_2(CH_3)_3 + AgI.$$

Caffeine, 1,3,7-*trimethyl-xanthine*, $C_8H_{10}N_4O_2$, occurs in both tea and coffee, from which it may be extracted. Coffee beans contain between 0·5 and 1 per cent. of caffeine; tea contains from 2 to 4 per cent. It is soluble to the extent of about one part in 80 of water, and crystallises from the solution in silky needles, which contain one molecule of water of crystallisation. It forms well characterised salts with acids, but these are largely hydrolysed when dissolved in water. It is practically without acidic properties. Caffeine itself and some of its salts are used in medicine, the salicylate and the bromide being most commonly employed.

Uric Acid, $C_5H_4N_4O_3$.

Uric acid is 2,6,8-trioxypurine, and has long been known as a constituent of human urine. The excrement of birds and serpents consists chiefly of urates. Uric acid may be prepared from guano by treatment with hot dilute sodium carbonate solution, which dissolves it, filtering the solution, and acidifying the filtrate with hydrochloric acid. From human urine, which normally contains less than 0·1 per cent. of uric acid, it may be obtained by saturating with ammonium chloride and adding a little concentrated ammonia solution. Ammonium urate, which is insoluble in concentrated ammonium chloride solutions, separates as a gelatinous precipitate from which the acid may be afterwards liberated.

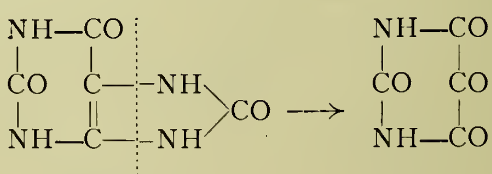
Uric acid occurs in the form of small rhombic crystals. It requires about 2000 parts of boiling water and 40,000 parts of cold water for its solution. It is insoluble in alcohol and ether, but dissolves readily in alkalies. It acts as a weak dibasic acid, the normal salts being unstable and passing readily into the acid salts, in which only one hydrogen has been replaced by a metallic radical. Its formula may be written—



Uric acid

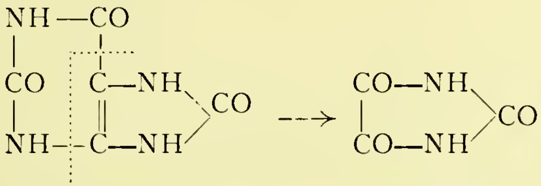
with the possibility of intermediate tautomeric forms. The formula consists of oxidised pyrazole and pyrimidine rings joined together with two carbon atoms in common.

When uric acid is oxidised with dilute nitric acid the pyrazole ring is broken, and an oxidised pyrimidine, **alloxan**, remains—



Uric acid Alloxan

When concentrated nitric acid is employed for the oxidation, it is possible to break the pyrimidine ring and leave an oxidised pyrazole, **parabanic acid**—



Uric acid Parabanic acid

By reduction of uric acid with sodium amalgam, xanthine is obtained.

The most characteristic test for uric acid is the **murexide test.** A small quantity of the acid is evaporated to dryness on a water-bath with a few drops of moderately concentrated nitric acid. A yellowish residue remains, which on the addition of ammonia assumes a fine purple colour, due to the presence of murexide, the ammonium salt of an alloxan derivative.

THE PROTEINS.

The substances known as proteins are extremely complex nitrogenous compounds, which occur both in animals and in plants. They may be looked upon in general as condensation products of various amino acids, for on hydrolysis they decompose chiefly with formation of such amino acids. Proteins are tasteless, inodorous solids exhibiting but little chemical activity. They dissolve in water or in dilute salt solutions, but the protein solutions so prepared are colloidal, the dissolved protein being unable to pass through animal or vegetable membranes, and showing the presence of particles when observed with the ultra-microscope. All protein solutions are optically active and lævo-rotatory. Although the proteins are thus colloids in the ordinary sense, some of them may be obtained in the crystalline form—for example, egg-albumin. The majority, however, are amorphous, and show no definite melting-point.

Since proteins are derived from amino acids they might be expected to be amphoteric in their nature. This is in reality the case, and the proteins are capable of forming unstable compounds both with acids and with bases. This amphoteric character is evident by the action of certain reagents in precipitating proteins. Thus protein solutions are precipitated by most salts of heavy metals—for example, copper sulphate or acidified mercuric chloride—the metal falling out of solution in combination with the protein, which, therefore, in this respect exhibits an acid character. On the other hand, picric acid and phosphotungstic acid precipitate proteins, which here show the behaviour of bases.

The formation of such precipitates as those mentioned above may be used in testing for proteins, but there are in addition certain colour reactions which are of value. Amongst these the

following may be noted as throwing some light upon the nature of the constituents of proteins.

I. **Biuret Reaction.**—If to a solution of egg-albumin or other protein, caustic soda is added, and then a few drops of dilute copper sulphate solution, a purple colour appears on mixing. This reaction is similar to that exhibited by biuret, and is therefore known as the biuret reaction. The proteins do not contain biuret, and the action is due to the presence of at least two CO.NH groups closely associated in the protein molecule (*cf.* 229).

II. **Xanthoproteic Reaction.**—When proteins are heated with concentrated nitric acid a yellow coloration is observed. Production of this yellow colour is due to the presence of aromatic rings in a protein molecule, which are converted into yellow nitro-derivatives by the nitric acid. The yellow stain produced by nitric acid on the skin has a similar origin.

III. **Millon's Reaction.**—Millon's reagent is a solution of mercuric nitrate with a trace of nitrite also present. It is made by dissolving mercury in concentrated nitric acid and diluting with water. With proteins, Millon's reagent yields a white precipitate, which becomes red on warming. This reaction points to the presence of a phenolic group in a protein molecule, as the reagent yields a red coloration with phenols.

IV. **Molisch's Test.**—This test indicates the presence of carbohydrate residue in a protein molecule. It is carried out as follows:—To the protein solution is added concentrated sulphuric acid and a little α-naphthol. A purple coloration appears, and is due to the action of α-naphthol on furfural, which is produced by the action of the sulphuric acid on a carbohydrate molecule.

Coagulation of Protein Solutions.—Many proteins are coagulated by heating their faintly acid solutions to the boiling-point, especially in presence of neutral salts such as sodium chloride. Thus the presence of albumin in the urine is detected by adding sodium chloride to filtered urine and heating. Insoluble phosphates may be precipitated along with albumin, but a few drops of acetic acid will dissolve these, and any albumin present will appear as a flaky precipitate.

Strong mineral acids coagulate proteins. **Heller's test** is performed by pouring the liquid to be tested carefully down

the side of a test-tube, so as to form a layer on the surface of a little concentrated nitric acid contained in the tube. A white ring of precipitate will form at the surface of separation if protein is present.

Neutral salts in high concentrations precipitate proteins in the cold. Ammonium sulphate and zinc sulphate are those most commonly used, and proteins may be classified according to the concentration of salt requisite for their precipitation. Thus whilst egg-albumin is only precipitated from a solution completely saturated with ammonium sulphate, serum-globulin is precipitated when the solution is only half saturated with the salt.

Hydrolysis of Proteins.

Proteins may be hydrolysed by means of water at a high temperature, more readily by dilute acids, and most readily at the body temperature by the action of certain enzymes, known generally as **proteases**, of which the pepsin of the stomach and the trypsin of the pancreatic juice may be taken as examples. The hydrolysis proceeds in stages, the products becoming less and less complex as the action progresses. The action may be comparated to the disintegrating hydrolysis of starch, where we have, for example, the stages :—

Starch → Soluble starch → Dextrins → Maltose → Glucose.

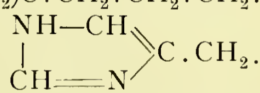
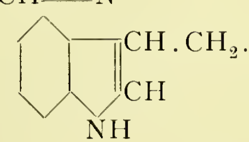
For proteins we have the hydrolysis scheme :—

Proteins → Metaproteins → Proteoses → Peptones → Polypeptides → Amino acids.

All the hydrolysis products except the amino acids give the biuret reaction. The amino acids are the chief ultimate hydrolysis units of the native proteins, and yield true solutions, which are assimilated by the animal body. The metaproteins, proteoses, peptones, still possess the properties of proteins, giving only colloidal solutions which are precipitated by saturation with ammonium sulphate, etc. The polypeptides may be prepared synthetically, and exhibit all degrees of complexity, the more complex giving the protein reactions, the simplest forming true solutions and giving no protein reactions.

Structural Units of the Proteins.

The amino acids are the chief structural units of the proteins, and these amino acids are all of the same type, having the amino group in the α-position with regard to the carboxyl group. They are thus all derivatives of glycine, $NH_2.CH_2.COOH$, and may for the most part be represented by the general formula $NH_2.\mathbf{C}HR.COOH$ or $R.\mathbf{C}H(NH_2).COOH$. The following table gives the names of the amino acids and the structural formulæ of the various groups represented by R.:—

Amino acid $R.CH(NH_2).COOH$	R.
Glycine (p. 254)	H.
Alanine	$CH_3.$
Serine	$HO.CH_2.$
Leucine	$(CH_3)_2CH.CH_2.$
Phenyl-alanine	$C_6H_5.CH_2.$
Tyrosine	p-$HO.C_6H_4.CH_2.$
Aspartic acid (p. 259)	$HOOC.CH_2.$
Glutaminic acid (p. 260)	$HOOC.CH_2.CH_2.$
Lysine	$NH_2.CH_2.CH_2.CH_2.CH_2.$
Arginine	$(NH)(NH_2)C.CH_2.CH_2.CH_2.$
Histidine (p. 283)	
Tryptophane (p. 286)	

Alanine, according to the above table, is $CH_3.\mathbf{C}H(NH_2).COOH$ —*i.e.*, α-amino-propionic acid ; aspartic acid is—

$$\begin{array}{l} \mathbf{C}H(NH_2).COOH \\ | \\ CH_2.COOH \end{array}$$

or α-amino-succinic acid.

Most natural proteins contain sulphur, which is a constituent

of a double amino acid, cystine, derived from two molecules of glycine, and containing the group—

$$\begin{array}{l} S.CH_2. \\ | \\ S.CH_2. \end{array}$$

equivalent to 2R. The formula of cystine is thus—

$$\begin{array}{l} S—CH_2.\mathbf{C}H(NH_2).COOH \\ | \\ S—CH_2.\mathbf{C}H(NH_2).COOH \end{array}$$

In some of the hydrolysis products of proteins the nitrogen atom of the amino group and the carbon atom of the CHR group form part of a ring. Thus we have—

$$\begin{array}{lcl} CH_2.CH_2. & & CH_2 \\ | & & | \\ NH & \text{———} & \mathbf{C}H.COOH \end{array}$$

Proline (p. 275)

in which a hydrogen of the amino group of glycine,

$$NH_2.CH_2.COOH,$$

and a hydrogen of the CH_2 group are replaced by the dyad radical $.CH_2.CH_2.CH_2.$

Although glycine itself is optically inactive, containing no asymmetric carbon atom, it will be observed that the derived α-amino acids, $NH_2.\mathbf{C}HR.COOH$, all contain one asymmetric carbon atom, and so may occur in optically active modifications. With the single exception of glycine, all natural proteins and their hydrolysis products actually exhibit optical activity.

The variety of natural proteins is very great, as might be inferred from the number of amino acids which form their structural units. No one protein, however, is known to contain all the amino acids mentioned. The chief amino acids in egg-albumin, for example, are alanine, glutaminic acid, leucine, phenyl-alanine, proline, lysine, and arginine. Gelatine contains glycine as principal amino acid with smaller quantities of arginine, proline, and hydroxyproline; aromatic amino acids are practically absent. Any mixture of proteins which can be utilised as food must yield a certain proportion of the aromatic amino acids tyrosine and tryptophane on hydrolysis within the body.

Synthetic Polypeptides.

The amino acids above mentioned and others of the same type may be condensed together with elimination of water to form polypeptides, which are known as dipeptides, tripeptides, etc., according to the number of amino acid residues they contain. There are various ways of effecting the condensation, but the scheme given below will serve to indicate the general principle followed.

The amino acid $NH_2.CHR.COOH$ may be converted into the acyl-chloride $NH_2.CHR.COCl$, which can then be made to interact with another amino acid, $NH_2.CHR'.COOH$, according to the following equation:—

$$NH_2.CHR.COCl + NH_2.CHR'.COOH$$
$$= NH_2.CHR.CO \vdots .NH.CHR'.COOH + HCl,$$

with formation of a dipeptide. This dipeptide is still an amino acid, and may now react with another amino-acyl chloride as follows:—

$$NH_2.CHR''.COCl + NH_2.CHR.CO \vdots .NH.CHR'.COOH$$
$$= NH_2.CHR''.CO \vdots .NH.CHR.CO \vdots .NH.CHR'.COOH + HCl.$$

In this way a tripeptide is formed, the dotted lines in the formula indicating the amino acid units. It should be noted that in carrying out the process in practice, the amino acid which reacts with the acyl-chloride must be in the form of an ester. The resulting polypeptide is therefore also an ester derivative, from which, however, the polypeptide itself may easily be prepared by hydrolysis. For simplicity the esterisation and ester-hydrolysis have been omitted in the above scheme.

The polypeptides are solids which are for the most part soluble in water (to give true or colloidal solutions according to their complexity), and nearly insoluble in alcohol. In contradistinction to the amino acids, which are generally sweet, the polypeptides are insipid or slightly bitter. The higher polypeptides give the biuret reaction, and are precipitated with the general reagents for proteins.

On boiling with concentrated hydrochloric acid the poly-

peptides are hydrolysed with re-formation of the amino acids, thus—

$$NH_2.CHR'.CO. \vdots NH.CHR.COOH + H_2O$$
$$= NH_2.CHR.COOH + NH_2.CHR'.COOH.$$

Pancreatic juice seems only to be capable of hydrolysing such polypeptides as yield the amino acid units which are found in the natural proteins.

Conjugated Proteins.

Certain proteins, *e.g.* the caseinogen of milk and the vitellin of egg-yolk, are distinctly acid in character, and are easily soluble in alkalies, being reprecipitated by addition of acids. When hydrolysed by means of caustic alkali they yield phosphates, and are termed in consequence **phospho-proteins.** The phosphoric acid thus obtained on hydrolysis must have formed part of the original molecule.

Besides the phospho-proteins, certain others exist in which the protein molecule is condensed or *conjugated* with molecules of a different class, the residue of which is usually called the *prosthetic group.* Thus we have the **chromo-proteins,** of which the most important is hæmoglobin. This consists of the protein globin conjugated with the pyrrole derivative hæmatin (p. 274). The **nucleo-proteins** contained in the cell-nuclei yield on complete hydrolysis, besides amino acids, phosphoric acid and purine derivatives (p. 291). The phosphorus of the nucleo-proteins is not split off from the rest of the molecule by means of alkali, as is the case with phospho-proteins. In the **glyco-proteins** the prosthetic group is a sugar or glucosamine residue (p. 238).

The **keratins** contained in hair, horn, hoofs, feathers, etc., are proteoid substances insoluble in water, dilute acid, or alkalies, and are unaffected by the usual body enzymes. On acid hydrolysis they yield amino acids. **Collagen,** the main constituent of cartilage, is partially hydrolysed on heating with water under pressure to form **gelatine,** a simpler protein which is manufactured on a large scale for use in cookery, photography, etc. It is soluble in water to form a colloidal solution, but may be rendered insoluble by treatment with formaldehyde. The gelatine capsules used in medicine consist of gelatine and glycerol.

LIPOIDS.

The term lipoid is used to indicate those fats or fat-like substances occurring in the organism which can be extracted by means of ether (or other solvent in which fats are soluble). The apparatus used for extracting these substances is known as a Soxhlet apparatus, and is shown diagrammatically in Fig. 22. The extraction apparatus S is attached on the one hand to the boiling-flask F, which contains the solvent, and on the other to the condenser C. The vapour from the boiling solvent passes upwards through the tube A, is condensed, and drops back on the dried tissue (mixed sometimes with sand or other absorbent) which is contained in a thimble of stout filter-paper, T. When a sufficient quantity of liquid has accumulated to reach the level of the top of the narrow tube B, it syphons back through this tube into the boiling-flask, carrying with it the fat it has extracted from the tissue. This process repeats itself automatically as the boiling is continued, till at last all the ether-soluble lipoids have been extracted. The boiling-flask is then detached from the extractor and the ether is distilled off. The residue consists of the fatty material, and may be weighed if the estimation of lipoid in a weighed quantity of tissue is desired.

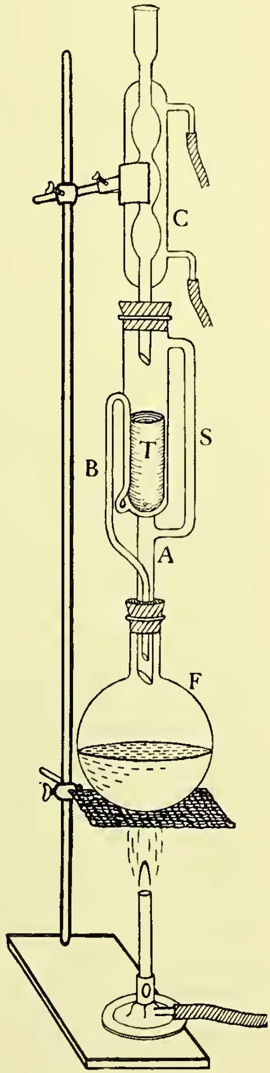


FIG. 22.

Besides the fats proper, the lipoids comprise the **cholesterols** (page 110), the **cerebrosides**, and a group of substances known as **phosphatides** or **phospho-lipines**.

Lecithin may be taken as a representative of the phosphatides. It is contained in practically all cells, and is found

abundantly in the brain and in egg-yolk. It is a waxy substance which melts at about 50°, is soluble in ether, alcohol, and benzene, giving solutions of a colloidal nature. With proteins it forms unstable compounds. On warming with baryta water it is hydrolysed with production of choline, of barium salts of the fatty acids proper, and of glycero-phosphoric acid. The same hydrolysis occurs under the action of certain enzymes. The constitution of lecithin may be represented thus—

$$\begin{array}{l} CH_2OOC.R \\ | \\ CH_2OOC.R \\ | \qquad\qquad /OH \\ CH_2.O.P\langle \\ \qquad\qquad\quad \backslash O.C_2H_4.N(CH_3)_3OH \end{array}$$

Lecithin

The products of hydrolysis are :—

$$\begin{array}{llll} & CH_2.OH & HOOC.R & \\ \text{Glycero-phosphoric acid (p. 143)} & | & & \text{Fatty acids} \\ & CH_2.OH & HOOC.R & \\ & | \qquad\qquad /OH & & \\ & CH_2.O.P\langle & HO.C_2H_4.N(CH_3)_3OH & \\ & \qquad\qquad \backslash OH & \text{Choline (p. 258)} & \end{array}$$

The acids R.COOH may be palmitic, stearic, or oleic acid, so that different lecithins exist.

The **cerebrosides** extracted from the brain contain nitrogen but no phosphorus. On hydrolysis they yield galactose (p. 200), complex bases, and fatty acids.

ALKALOIDS.

The alkaloids are nitrogenous bases which generally occur in plants in the form of salts of organic acids. The purine bases are frequently included amongst the alkaloids, but since they differ in many of their properties from the more characteristic alkaloids, they have been treated in a separate section (p. 291). The alkaloids may be found in various parts of the plant, but the fruit, seeds, and occasionally bark and leaves are the most important sources.

To extract the alkaloids, the finely divided material is treated with dilute hydrochloric or sulphuric acid. These acids expel the organic acids and form chlorides or sulphates of the alkaloids, which dissolve in water. Addition of alkali to the solution of the salt precipitates the alkaloids, which are usually very sparingly soluble. Crystallisation of the alkaloids or of their salts is used for further purification.

The great majority of the alkaloids are solid, and contain oxygen in addition to carbon, hydrogen, and nitrogen. The liquid alkaloids, coniine and nicotine, contain no oxygen. Although very sparingly soluble in water, the alkaloids dissolve readily in alcohol, less readily in ether or chloroform. Many of their solutions have a strongly alkaline reaction, and practically all exhibit optical activity, commonly with lævo-rotation. Their salts are generally well defined and crystalline.

Precipitates are formed when aqueous solutions of the alkaloids or their salts are treated with the following reagents:—

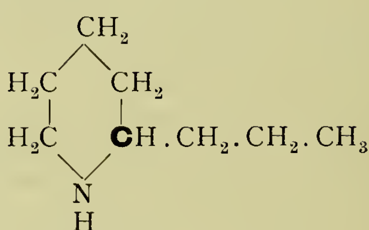
Iodine in potassium iodide,
Potassium mercuric iodide,
Phospho-molybdic acid,
Tannin,
Picric acid.

These and other reagents yield sparingly soluble compounds with aqueous solutions of the alkaloids or their soluble salts, but it must be borne in mind that many other organic substances besides the alkaloids are precipitated by the same reagents. Thus, iodine in potassium iodide will give a brown precipitate of a periodide with quinoline, which is indistinguishable in appearance from that given with an alkaloid.

LIQUID VOLATILE ALKALOIDS.

Coniine, $C_8H_{17}N$, occurs with other alkaloids in the spotted hemlock (*Conium maculatum*), especially in the seeds. It is a colourless liquid which boils at 167°, and is only sparingly soluble in water. It acts as a monacid base, its chloride, for example, having the formula $C_8H_{17}N,HCl$. The salts are readily soluble in water, and like the base itself are extremely poisonous.

Coniine was the first alkaloid to be prepared synthetically, and is known to be α-propyl-piperidine—

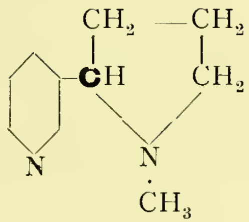


Coniine

The natural base is optically active and dextro-rotatory, the carbon atom to which the propyl group is attached being asymmetric.

Nicotine, $C_{10}H_{14}N_2$, occurs in tobacco leaves as malate and citrate, the dried leaves containing about 0·8 per cent. of the alkaloid. It is a colourless liquid which boils at 245° with decomposition, but unlike coniine it is easily soluble in water. It is slightly heavier than water, and may be recognised by its pungent odour. It is a diacid base, but the salts do not generally crystallise well. The base is lævo-rotatory and highly poisonous.

Nicotine has been prepared synthetically, and is known to have the following constitution :—



Nicotine

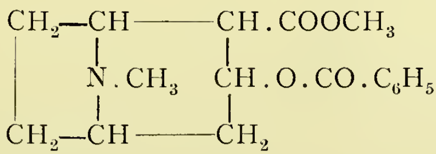
It thus consists of a pyridine ring and a methyl-pyrrolidine ring joined together.

SOLID NON-VOLATILE ALKALOIDS.

The alkaloids containing oxygen are generally much more complex in their structure than the volatile alkaloids described above. Only one or two can be detailed here.

Cocaine, $C_{17}H_{21}NO_4$.

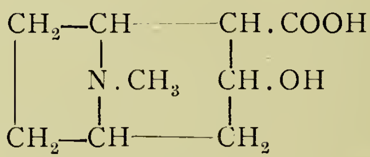
Cocaine occurs together with other alkaloids in coca-leaves. It is a crystalline solid which melts at 98°. It is sparingly soluble in water, but its chloride, $C_{17}H_{21}NO_4,HCl$, is readily soluble, and is employed in medicine as well as the free base. The chief use of cocaine is as a local anæsthetic. The formula of cocaine is—



I. II.

If we consider this formula we see that it may be looked upon as consisting of a 7-carbon ring with a nitrogen bridge across it. Such bridged rings are common amongst the alkaloids, and we have already seen examples of them in the terpenes (p. 215).

Looking at the smaller rings, we find that the nitrogen ring marked I. is a pyrrolidine ring, whilst that marked II. is a piperidine ring. These two rings have the group $.CH.N(CH_3).CH.$ in common. Besides this it is evident that cocaine is the methyl ester of an acid, since it contains the group $COOCH_3$; and that it is the benzoate of a complex alcohol, since it contains the grouping $C_6H_5.CO.OR$. Thus when cocaine is hydrolysed by means of dilute acids it gives rise to methyl alcohol, benzoic acid, and the acid-alcohol **ecgonine**—

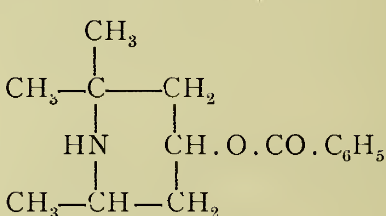


Ecgonine

From ecgonine cocaine can easily be regenerated by introduction of the methyl and benzoyl groups instead of hydrogen.

Local Anæsthetics.

The group $\mathrm{N{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}O.CO.C_6H_5}$ contained in cocaine occurs in the synthetic substance **eucaine**—



β-Eucaine

the salts of which have been used as local anæsthetics.

Other local anæsthetics which have been synthetically prepared contain the similar group—

$$\mathrm{\overset{|}{\underset{|}{N}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}O.CO.C_6H_5.}$$

Thus we have the following substances :—

Stovaine, the chloride of the base—

$$\begin{array}{lllll} CH_3 & & H & CH_3 & \\ | & & | & | & \\ N & — & C — & C — & O \,.\, CO \,.\, C_6H_5 \\ | & & | & | & \\ CH_3 & & H & C_2H_5 & \end{array}$$

Alypine, the chloride of the base—

$$\begin{array}{lllll} CH_3 & & H & C_2H_5 & \\ | & & | & | & \\ N & — & C — & C — & O \,.\, CO \,.\, C_6H_5 \\ | & & | & | & \\ CH_3 & & H & CH_2 & \\ & & & | & \\ & & & N(CH_3)_2 & \end{array}$$

Novocaine, the chloride of the base—

$$\begin{array}{lllll} C_2H_5 & & H & H & \\ | & & | & | & \\ N & — & C — & C — & O — CO \,.\, C_6H_4 \,.\, NH_2 \text{ (para)} \\ | & & | & | & \\ C_2H_5 & & H & H & \end{array}$$

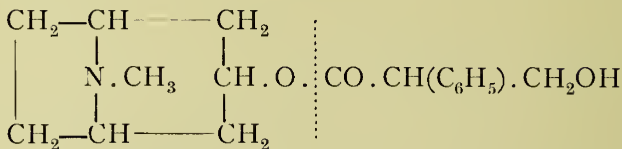
This group of local anæsthetics illustrates well the fact that a certain type of chemical constitution often gives rise to a definite physiological action.

Atropine, $C_{17}H_{23}NO_3$.

Atropine, the alkaloid contained in deadly nightshade (*Atropa belladonna*), differs from most alkaloids in being an optically inactive racemic substance. The lævo-rotatory form of the same substance is found in the alkaloid **hyoscyamine** from henbane (*Hyoscyamus niger*).

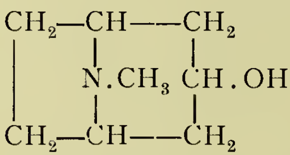
Atropine is a powerful poison, and has the property of dilating the pupil when applied in solution to the eye, for which reason it is extensively used in ophthalmology.

The constitutional formula of atropine is written as follows :—



Atropine

The ring structure which it contains is the same as that found in cocaine and ecgonine, and it is plain from the formula that atropine is an ester. Consequently on hydrolysis it splits at the dotted line and yields the following products :—



Tropine

$HOOC.CH(C_6H_5).CH_2OH$

Tropic acid

It will be observed that ecgonine is a carboxyl-derivative of tropine.

Quinoline Group of Alkaloids.

This group contains the important alkaloids, quinine and cinchonine, derived from cinchona bark, and also strychnine and brucine, derived from nux vomica.

Quinine, $C_{20}H_{24}N_2O_2$, may be extracted along with other cinchona alkaloids from the bark by means of dilute sulphuric acid, and purified by recrystallisation of the sulphates from water, quinine sulphate being sparingly soluble. Or the base itself may be liberated from the bark by lime, and extracted with boiling petroleum. The petroleum solution of bases is then treated with excess of dilute sulphuric acid to form acid sulphates, which dissolve in water. Neutralisation with sodium carbonate yields crystals of quinine sulphate on cooling.

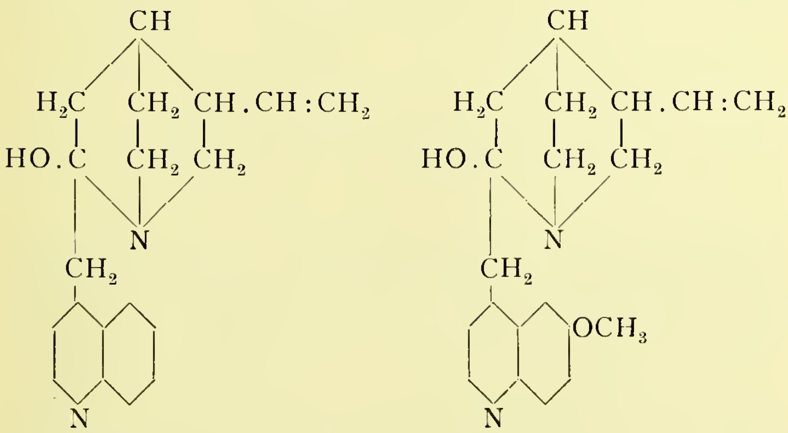
Quinine is one of the most important natural drugs. It is used as a tonic, and to lower the body temperature in malaria, etc.

Quinine acts as a diacid base, and many of its salts are employed in medicine. It requires for its solution about 2000

parts of water, from which it crystallises as a trihydrate; but it is very soluble in alcohol, and freely in chloroform or ether. The normal sulphate is only about twice as soluble in water as the base itself, but the acid sulphate is about 200 times as soluble as the base, and is therefore much used.

Cinchonine, $C_{19}H_{22}N_2O$, is prepared from the sulphate mother liquors obtained in the extraction of quinine. The base and its salts are less active physiologically than the corresponding quinine compounds.

The constitutional formulæ of quinine and cinchonine have not been established with the same certainty as those of the alkaloids previously described. The following formulæ are perhaps the most probable:—



Cinchonine Quinine

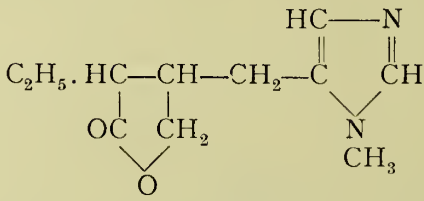
These formulæ show quinine to be a methoxy-derivative of cinchonine.

Strychnine, $C_{21}H_{22}N_2O_2$, and **Brucine,** $C_{23}H_{26}N_2O_4$, are both obtained from nux vomica. They act as monacid bases, and contain an oxidised quinoline ring. Strychnine is a powerful poison, and is administered in very small doses as a bitter and tonic. Brucine is much less active physiologically and is probably a dimethoxy-derivative of strychnine.

Pilocarpine, $C_{11}H_{16}N_2O_2$.

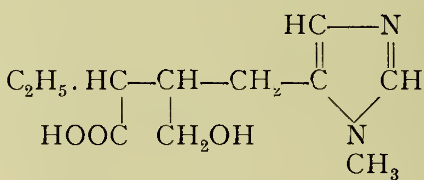
This is the chief alkaloid found in jaborandi. If differs from

most of the solid alkaloids in being easily soluble in water and only slightly soluble in ether. Its constitutional formula is—



Pilocarpine

The nitrogen ring is that of imidazole (p. 283): the oxygen ring is that of the lactone of a γ-hydroxy acid. When, therefore, caustic alkali in excess is added to pilocarpine, the oxygen ring is broken and a salt of **pilocarpic acid**—

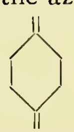
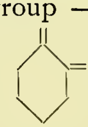
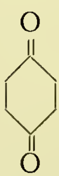
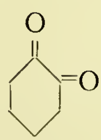


is produced. The strong physiological action of pilocarpine, which is opposed to that of atropine, is destroyed when the lactone ring is thus broken.

DYES, STAINS, AND INDICATORS.

By a dye is meant not merely a coloured substance, but one which can be absorbed by a fibre or tissue, and be held so firmly that it cannot be removed by ordinary treatment with water, or with weak alkalies, such as soap solutions. A dye should also have the property of fading only slowly when exposed to light. Dyes which fulfil these requirements are said to be *fast* to washing and to light.

Most dyes are complex in their chemical constitution, the complexity and large size of the molecule being no doubt an essential condition for the absorption by the fibre and resistance to the solvent action of water. All absorbable dyes are either acidic or basic in their character. Purely neutral substances, even when coloured, never act as such dyes, unless they are amphoteric substances, and owe their neutrality to a balancing of acidic and basic properties in the molecule. Salts of acids or bases which become hydrolysed when dissolved in water are frequently used as dyes.

The colour of ordinary dyes is generally due to the presence of certain definite groups of atoms in the molecule. Such groups are called **chromophore groups,** the most important being the nitro group —NO_2, the azo group —N : N—, and the so-called quinonoid grouping  or  resembling that found in para-quinone  and ortho-quinone  (p. 168). The substance containing these groups is said to be a **chromogen,** and is almost invariably coloured; but unless certain other groups, which do not themselves confer colour, are present at

the same time, the substance has no tinctorial properties. Thus nitrobenzene, $C_6H_5 . NO_2$, azobenzene, $C_6H_5 . N : N . C_6H_5$, and the quinones are coloured, but are not dyes, the reason being that they are neither acidic nor basic. As soon, however, as an acidic or basic group, such as —OH (phenolic hydroxyl), —NH_2, or —SO_3H, is introduced, the chromogen acquires an acid or basic character and becomes an absorbable dye. Such groups are said to be **auxochrome groups**.

Thus in methyl-orange, which is—

the sodium salt of dimethylamino-azobenzene-sulphonic acid, the azo group . N : N ., is the chromophore group; azobenzene, $C_6H_5 . N : N . C_6H_5$, is the chromogen, and the dimethylamino and sulphonate groups are the auxochrome groups.

Dyes are conveniently classed for certain practical purposes as acid or basic dyes. Acid dyes generally stain fibres or tissue elements of basic character, whilst basic dyes generally stain fibres or tissue elements of acid character. From this it must not be concluded that the process of staining or dyeing is purely chemical in its nature; absorption and colloidal behaviour play a great part in the process. It is well to remember, however, that certain chemical affinities of the ordinary type are prerequisite for dyeing.

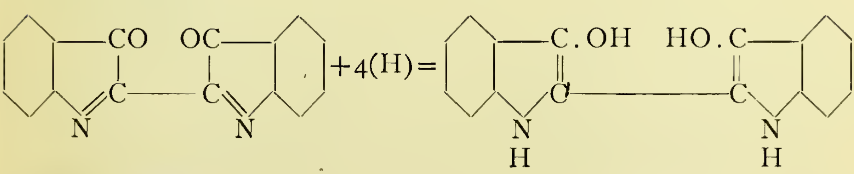
Acid dyes are those that contain phenolic groups, often associated with nitro groups, or those that contain sulphonic acid groups along with amino groups. Basic dyes contain amino or replaced amino groups, generally as chlorides, sulphonic groups being absent. Methyl orange is thus, in the above sense, an acid dye.

Another classification which is of importance in histological work is connected with the complexity of the molecule of the dyes, which may be divided roughly into three classes according to the ease with which they pass through a parchment-paper membrane. The diffusible dyes (which generally contain less than fifty atoms in the molecule) pass through with comparative rapidity. Examples of such dyes are eosine, picric acid, Bismarck brown. The colloidal dyes (which generally contain over seventy atoms in the molecule) give solutions which are

precipitated by small quantities of salts and scarcely pass through the membrane at all. Congo red is an example of such a dye. There is an intermediate group of semi-colloidal dyes which pass slowly through the membrane, examples of which are fuchsine and methyl violet. In histology it is only the diffusible and semi-colloidal dyes that are of practical importance as stains; the colloidal dyes cannot pass through the animal or vegetable membranes of the cell, and are thus unable to stain the cell contents.

Sometimes when a dye will not directly colour a fibre or tissue, it may be made to do so by the intervention of a substance known as a **mordant.** Thus if cotton is soaked in a solution of the basic dye magenta or fuchsine it does not take up the colour, but if the cotton is first mordanted by soaking in a solution of tannic acid, it is then capable of taking up and firmly binding the dye. The neutral cellulose of which cotton consists can absorb tannic acid from its colloidal solution in water and retain it firmly. This action is not chemical, and may be compared to the absorption of ammonia gas or tarry matter by charcoal. The tannic acid on the fibre can now take up the basic magenta and fix it in the fibre as an insoluble compound which cannot be removed by washing. Tannic acid is here an example of an acid mordant. Aluminium salts and ferric salts of weak acids are good examples of basic mordants, hydrolysis producing from them colloidal bases which are absorbed by the fibre or tissue. The insoluble coloured substances produced by the action of mordant and colouring matter are called **lakes.** Alizarin (p. 187) is an instance of an acid dye constantly used in conjunction with basic mordants.

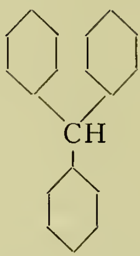
Indigo (p. 287) is not an absorbable dye, since it has neither acid nor basic properties and is insoluble in water, dilute alkalies, and acids. In order that a fibre may be dyed with it, the indigo is first reduced by means of sodium hydrosulphite to indigo white—



Indigo blue   Indigo white

Indigo white, although a colourless substance, is, owing to the phenolic groups, absorbable by fibres from alkaline solution. When the impregnated material is exposed to air, the indigo white is gradually re-oxidised to indigo blue, which is thus produced as an insoluble substance in the interior of the fibre.

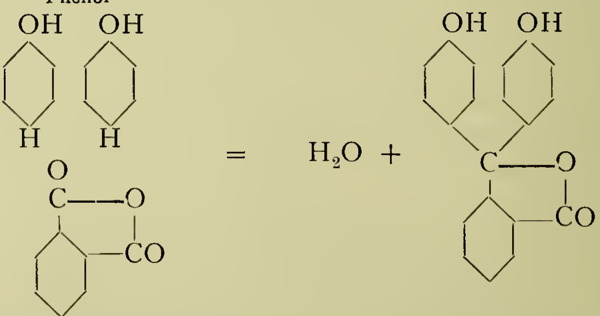
In the following sections, examples of the three important classes of phthalein, rosaniline, and azo dyes are given, selected chiefly owing to their use as indicators or as stains in histological work. The two classes of phthalein and rosaniline dyes are often spoken of together as triphenylmethane dyes, since they may be regarded as derivatives of triphenylmethane, $CH(C_6H_5)_3$, the graphic formula of which is—



Triphenylmethane

Phthalein Dyes.

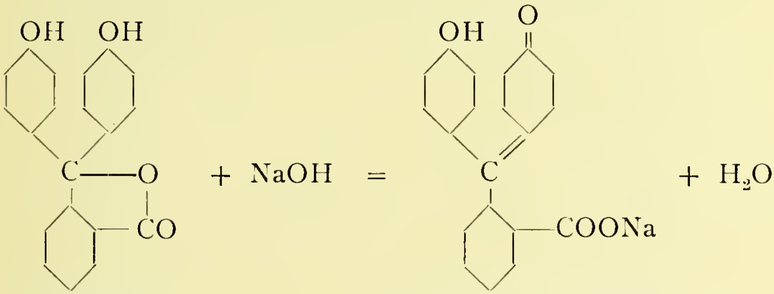
When phenol is heated with phthalic anhydride in presence of a dehydrating agent, such as sulphuric acid or anhydrous zinc chloride, water is given off and **phenolphthalein** is produced (p. 179). The action may be conceived as follows:—



Phthalic anhydride Phenolphthalein

Phenolphthalein is itself practically colourless, but when alkali

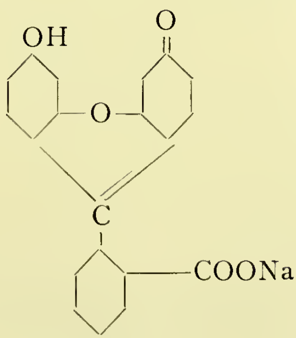
is added to its solution it assumes a bright pink colour, whence its use as an indicator. The constitution generally attributed to its sodium salt is shown in the following equation :—



Phenolphthalein　　　Sodium salt of phenolphthalein

In the passage from the phthalein to its salt an isomeric change in constitution is supposed to occur, the quinonoid structure, and consequently colour, appearing.

Fluorescein is a phthalein formed from resorcinol, m-$C_6H_5(OH)_2$, and phthalic anhydride. The formula of its sodium salt is as follows, when written with the quinonoid structure :—



Sodium salt of fluorescein (Uranin)

Uranin exhibits a brilliant greenish fluorescence in solution, but is of little importance as a dye.

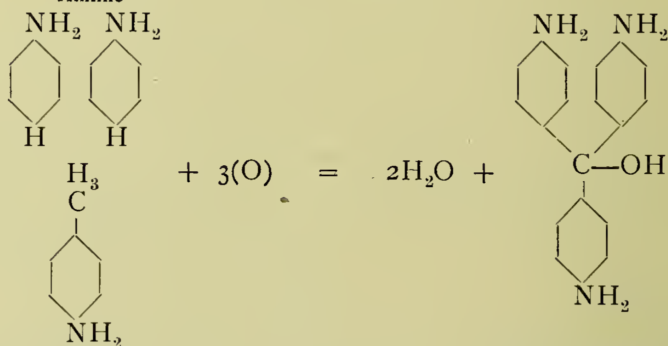
The **eosins** are in general fluoresceins in which several hydrogen atoms of the rings are replaced by bromine or iodine. Ordinary eosine-A is tetrabromo-fluorescein. The eosins are largely used as reddish dyes and stains.

The phthaleins are all acid dyes.

Rosaniline Dyes.

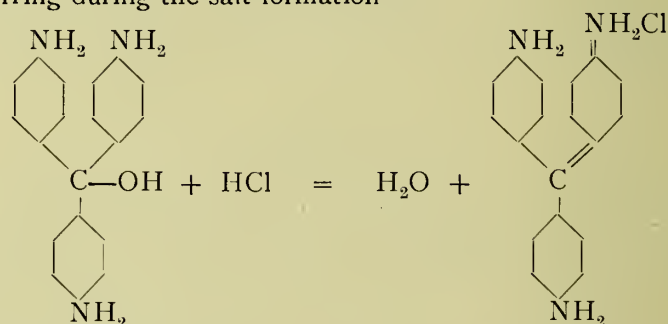
When a mixture of aniline and *p*-toluidine is oxidised with a mild oxidising agent, the following synthesis occurs :—

Aniline



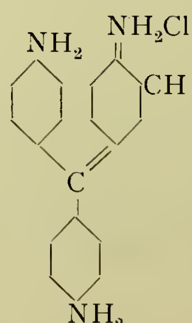
p-Toluidine Base of pararosaniline

On addition of hydrochloric acid to this colourless base a coloured chloride is obtained, a change to quinonoid structure occurring during the salt-formation—



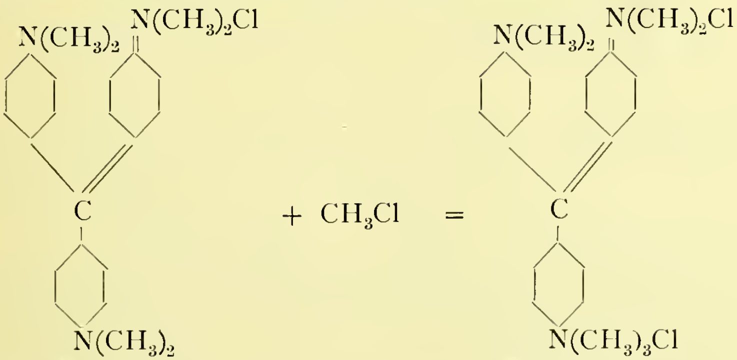
Base of pararosaniline Pararosaniline chloride

Fuchsine, or magenta, is a methyl-derivative of para-rosaniline chloride, the methyl being in the ortho position to the chloride group—



Fuchsine

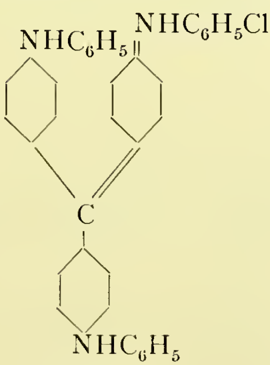
The **methyl violets** are prepared by the use of dimethyl-aniline, and are methyl-derivatives of pararosaniline chloride, four, five, or six atoms of hydrogen attached to the nitrogen atoms being replaced by methyl groups. The hexamethyl-derivative has the constitution given below—



Methyl violet   Methyl green

Methyl green is prepared by the addition of methyl chloride to methyl violet.

Aniline blue is a triphenyl-rosaniline chloride—



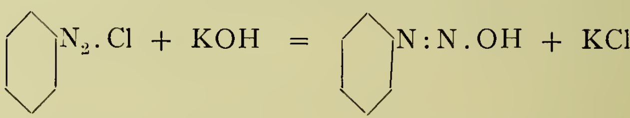
Aniline blue

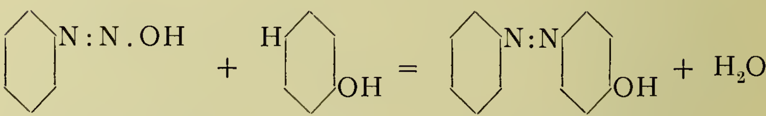
All these dyes are basic in character and are used in histology as basic stains.

If it is desired to have a similar dye but with acidic character, the transformation may be affected by introducing a sulphonic acid group. Thus **acid fuchsine**, used as a histological stain, is the acid sodium salt of the disulphonic acid obtained by the sulphonation of fuchsine.

Azo Dyes.

When diazobenzene chloride (p. 260) is mixed with phenol in presence of alkali, the following interaction takes place:—

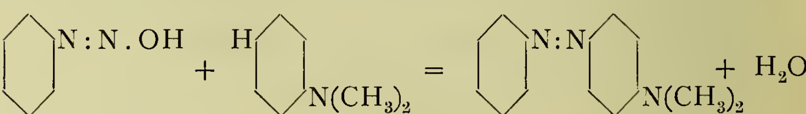




Diazobenzene hydroxide Phenol Hydroxyazobenzene

The hydrogen in the para position to the hydroxyl in the phenol unites with the hydroxide group of the base, and an azo compound is formed.

Similarly, when dimethylaniline is employed instead of phenol, the following reaction occurs:—



Diazobenzene hydroxide

Again, the hydrogen in the para position to the dimethylamino group is that which reacts.

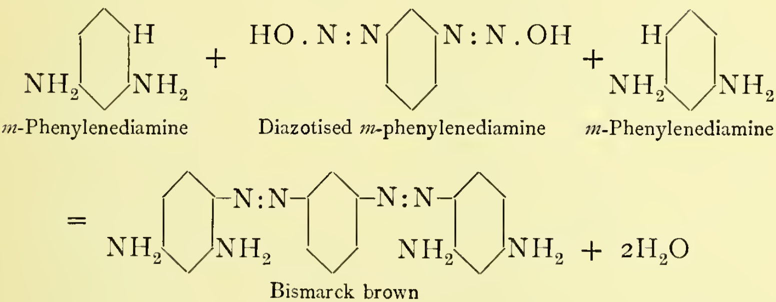
Neither of the above azo compounds is a satisfactory dye, but the dimethylamino compound is used in physiological chemistry as an indicator in titrating acid mixtures, *e.g.*, the stomach contents.

Methyl orange, used as an indicator for strong acids with weak bases, is the sodium salt of a sulphonic acid derivative of dimethylamino-azobenzene—

Methyl orange

It is prepared by diazotising sulphanilic acid, p-$HSO_3.C_6H_4.NH_2$, and coupling the diazo compound with dimethylaniline.

Bismarck brown, one of the oldest azo dyes, and a useful histological basic stain, is made by treating *m*-phenylenediamine with nitrous acid. One molecule of the base is fully diazotised and couples up with two other molecules to form a double azo or diazo compound.



Owing to this reaction, *m*-phenylenediamine is a delicate reagent for the detection of traces of nitrites in water. The base is dissolved in dilute sulphuric acid and a little of the solution is added to the water to be investigated. If even traces of nitrites are present, a brown or yellow colour, due to the production of Bismarck brown, soon appears.

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